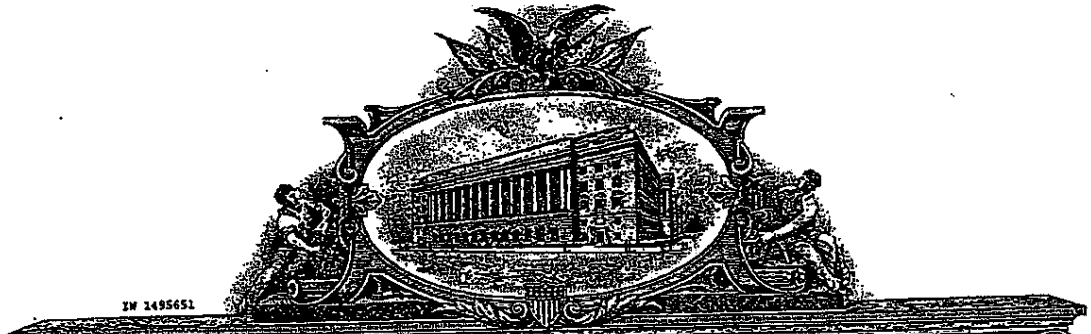
EXHIBIT G



IW 1495651

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August 23, 2006

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By Authority of the
Under Secretary of Commerce for Intellectual Property
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N. WILLIAMS
Certifying Officer

09/248536

ISSUE CLASSIFICATION	
Class	Subclass
604	232

[redacted]

PATENT NUMBER
6562011

U.S. UTILITY PATENT APPLICATION

O.I.P.E.	PATENT DATE
Dup SCANNED 1 G Q.A.	MAY 13 2003

SECTOR	CLASS	SUBCLASS	ART UNIT	EXAMINER
	604	232	~~3764~~ 3763	Simmons

FILED WITH: ☐ DISK (CRF) ☐ FICHE
(Attached in pocket on right inside flap)

See 09/349,748

PREPARED AND APPROVED FOR ISSUE

ISSUING CLASSIFICATION

ORIGINAL		CROSS REFERENCE(S)						
CLASS	SUBCLASS	CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					
604	232							
INTERNATIONAL CLASSIFICATION								
A61M 5/00								
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/								
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☐ Continued on Issue Slip Inside File Jacket

☐ TERMINAL DISCLAIMER	DRAWINGS			CLAIMS ALLOWED	
	Sheets Drwg.	Figs. Drwg.	Print Fig.	Total Claims	Print Claim for O.G.
	2	4	1	7	1
☐ a) The term of this patent subsequent to ________ (date) has been disclaimed.	Kevin C. Simmons (Assistant Examiner) (Date)			NOTICE OF ALLOWANCE MAILED: 9-20-02	
☐ b) The term of this patent shall not extend beyond the expiration date of U.S Patent. No. ________	BRIAN L. CASLER SUPERVISORY PATENT EXAMINER TECHNOLOGY CENTER 3700 Brian L. Casler (Primary Examiner) 9/6/02 (Date)			ISSUE FEE: Amount Due $1280.00	Date Paid 12-16
☐ c) The terminal ___ months of this patent have been disclaimed.	J Green (Legal Instruments Examiner) 9-25-02 (Date)			ISSUE BATCH NUMBER	

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Form PTO-436A (Rev. 6/99)

FORMAL DRAWINGS (___ SETS) SET

ISSUE FEE IN FILE

(LABEL AREA)

DRAWINGS IN FILE

ISSUE FEE IN FILE

(FACE)

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
09/348,536	07/07/99	604	3734	5637.200-US

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CONTINUING DOMESTIC DATA********
VERIFIED PROVISIONAL APPLICATION NO. 60/098,702 09/01/98
Yes KCS

371 (NAT'L STAGE) DATA********
VERIFIED KCS
None

FOREIGN APPLICATIONS********

VERIFIED			
KCS	DENMARK	PA 1998 00909	07/08/98
Yes	DENMARK	PA 1998 01500	11/17/98

IF REQUIRED, FOREIGN FILING LICENSE GRANTED 08/03/99

Foreign Priority claimed 35 USC 119 (a-d) conditions met / Verified and Acknowledged (Examiner's initials)	Met after Allowance (Initials)	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☒ yes ☐ no / ☒ yes ☐ no	☐	DEX	2	25	2

#26

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TITLE: MEDICATION DELIVERY DEVICE

FILING FEE RECEIVED	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT NO. _____ for the following:	
$980		☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

PATENT APPLICATION SERIAL NO. _____

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

07/20/1999 HPEOPLES 00000053 141447 09348536
01 FC:101 760.00 CH
02 FC:103 90.00 CH

PTO-1556
(5/87)

*U.S. GPO: 1998-433-214/80404

The present invention relates to a medication delivery device having a cartridge and a dosing assembly coupled together for delivering selected doses of medication, wherein at least one of the coupling means of the cartridge is unitarily moulded with the cartridge.

Background

Some medication, such as insulin is self-administered. The typical diabetes patient will require injections of insulin several times during the day. The required insulin dose will vary from patient to patient, and will for each patient often also vary during the day. Each patient will often establish a regimen for the insulin administration adjusted to his or her insulin need as well as lifestyle. Medication delivery pens have been developed to facilitate the self-administration of medication, such as insulin.

One prior art medication delivery pen includes a pen body assembly comprising a medication cartridge and a plunger device. A needle assembly may be connected to the pen body assembly. The medication is delivered by moving or pressing a plunger in the direction of the needle assembly thereby delivering the medication. When the medication in the cartridge is exhausted the pen body assembly is discarded. Depending on the medication needs for each individual the medication in the cartridge will last for several days. During this period the needle assembly will often have to be replaced by a new assembly or new needle due to increasing bluntness of the needle making injections painful for the patient.

More recent developments have revealed medication delivery pens, wherein the cartridge holder assembly can be disassembled from the pen body assembly after the medication therein has been exhausted, discarded and replaced by a new medicine-containing cartridge assembly.

An example of this is shown in EP 0 688 571 disclosing a medication delivery pen having a reusable pen body assembly and a disposable cartridge assembly that are threadedly engageable with one another. The cartridge assembly comprises a cartridge, a cartridge housing, a cap between the distal end of the cartridge and the housing, securing the cartridge in the housing and being adapted for engagement

with a needle assembly. Furthermore, the cartridge comprises a plunger within the cartridge. The reusable pen body assembly is coupled through a threaded coupling to the cartridge housing. Thus, the total number of parts comprising the prior art cartridge assembly is high.

It is an object of the present invention to provide a medication delivery device wherein the amount of parts of the cartridge is minimised.

Summary of the invention

Accordingly, the present invention relates to a medication delivery device comprising a cartridge assembly, a dosing assembly and optionally a needle assembly,

said cartridge assembly having one end sealed with a pierceable sealing, said end of the cartridge assembly comprising coupling means for engaging a needle assembly, and another end comprising coupling means for engaging the dosing assembly, said cartridge assembly further comprising a cartridge wherein at least one of the coupling means of said cartridge assembly is unitarily moulded with the cartridge, the cartridge further comprising a stopper adapted to receive plunger means, and

said dosing assembly comprising plunger means has coupling means for engaging the cartridge assembly, and said plunger means is adapted to engage the stopper of the cartridge when the dosing assembly is coupled to the cartridge.

The unitarily moulded coupling(s) ~~secure(s)~~ or couplings ensure that the coupling is not accidentally released from the cartridge during use and storage. Also, the above-described medication delivery device has fewer parts that the prior art devices because at least one coupling means is moulded unitarily with the cartridge. Thereby the costs involved in the production and assembling of the device are reduced, and the device is more economical; which is an important feature for a disposable device.

The medical delivering device may either be manufactured as a disposable device which is sold pre-filled with the insulin or it may appear as a durable medical delivering device so designed that it can receive disposable cartridges with insulin.

In a preferred embodiment the dosing assembly is reusable and the cartridge assembly is disposable, and accordingly, a second aspect of the present invention is a medication delivery device wherein the dosing assembly is releasably coupled to the cartridge assembly.

The medication delivery device is preferably constructed so as to ensure that the plunger means abuts on the stopper during use of the device, such as attaching and releasing the needle assembly. It is understood that the plunger means must disengage the stopper when the cartridge assembly is deliberately released from a reusable dosing assembly because the medication in the cartridge has been exhausted and the cartridge assembly is to be discarded. In this situation the plunger means is to be retracted to the dosing assembly before assembling the device with a new cartridge assembly.

Securing the abutment of the plunger means on the stopper during use of the medication delivery device, in particular when the needle assembly is coupled to and/or decoupled from the cartridge assembly, may be carried out by a variety of means. In a preferred embodiment the abutment is secured by preventing the cartridge assembly from being inadvertently released from the dosing assembly.

In particular, when the cartridge assembly is released from the dosing assembly through a movement including an axial movement, such as through a threaded coupling, it is preferred that the means for releasably coupling the needle assembly and the cartridge assembly together are such that the coupling and/or decoupling of the needle assembly cannot cause an axial movement of the cartridge assembly with respect to the dosing assembly. Thus, in that respect examples of the preferred couplings between the needle assembly and the cartridge assembly include releasable snap locks. Another preferred embodiment includes a safety on the coupling between the dosing assembly and the cartridge assembly, such as hinge on the

coupling or a threaded coupling releasable only after exerting an axial pressure on the coupling.

A second aspect of the present invention is a cartridge assembly for use in a medication delivery device, said cartridge assembly having one end sealed with a pierceable sealing, said end of the cartridge assembly comprising coupling means for engaging a needle assembly, and another end comprising coupling means for engaging the dosing assembly, said cartridge assembly further comprising a cartridge wherein at least one of the coupling means of said cartridge assembly is unitarily moulded with the cartridge, said cartridge further comprising a stopper.

The cartridge assembly may further comprise a cartridge housing for protecting the cartridge in use. Furthermore, when the cartridge is moulded unitarily with one coupling means the cartridge housing may comprise the other coupling means. Accordingly, in one embodiment of the invention the housing of the cartridge assembly comprises coupling means for coupling the cartridge assembly to the dosing assembly, preferably the coupling means is moulded unitarily with the housing. The cartridge is arranged within the cartridge housing. The cartridge housing may be non-releasably attached to the cartridge, once the cartridge is arranged in the housing, whereby the housing is disposed with the cartridge. In another embodiment the housing is reusable and the cartridge is arranged releasably in the housing.

In a preferred embodiment all the coupling means of the cartridge assembly are unitarily moulded with the cartridge. Thereby, it is possible to construct the cartridge assembly without the housing providing a cartridge assembly with even fewer parts.

The coupling means of the cartridge assembly may be for any suitable coupling, preferably a releasable coupling. Examples of the coupling are snap locks, such as snap locks with guidewire and sideways snap locks, snap locks released through threads, bajonet locks, luer locks, hinged locks, threaded locks and any suitable combinations thereof.

The coupling means unitarily moulded with the cartridge are preferably external coupling means, such as an external threaded coupling.

In particular the coupling means for engaging to the dosing means may be an external threaded coupling.

The cartridge may be moulded from any material suitable for medical containers. The cartridge is preferably moulded from a plastic material, e.g. by injection moulding. A suitable choice of material allows the cartridge to be at least partly transparent, whereby the user can see whether content, such as liquid is left in the cartridge. In a preferred embodiment the cartridge is totally transparent giving the user a greater possibility of inspecting the content of the cartridge.

By using a plastic material as compared to the usual glass material a great advantage is achieved in the production lines. Normally a significant quantity of the produced glass cartridges will be spoiled in the lines due to breakage, however the loss is greatly reduced by the use of plastic cartridges. Furthermore, the risk of small loose glass particles in the cartridges have been eliminated.

Also, by moulding the coupling(s) unitarily with the cartridge a very precise coupling mechanism may be obtained, since no further steps are to be taken to attach coupling means to the cartridge.

The cartridge may be of any suitable form, such as a cylinder. The cylinder may be constructed with various combinations of circular or non-circular inner and outer cross-section. In another embodiment the cartridge may be box-shaped having essentially rectangular or triangular cross-section.

The stopper is in sliding fluid tight engagement in the cartridge. The stopper is preferably made of plastic and/or rubber material.

The flexibility of the cartridge wall is not critical, however if the cartridge is too flexible the function of the stopper may be impaired. Mostly, the cartridge is made of a material only slightly flexible to non-flexible.

In order to enforce and strengthen the cartridge wall the cartridge may be integrally moulded with reinforcements. Thereby, the necessity of a protective housing may be

obviated. Furthermore, a scale may be integrally moulded with the cartridge wall providing the user with a measure for the medication used and left.

In a most preferred embodiment the cartridge assembly is comprised only of a cartridge being sealed in one end with a sealing, being unitarily moulded with all couplings means and comprising a stopper.

In a cylindrical cartridge the two couplings of the cartridge assembly are generally opposing each other having the same axis. However, the coupling for engaging with the dosing assembly being separate from coupling for engaging the needle assembly may be arranged so that their axis are in any angle with respect to each other, such as perpendicular, or even parallel, but not overlapping .

Another aspect of the present invention is a cartridge being at least partly filled with liquid medication, such as insulin.

In another embodiment the invention relates to a medication delivery device for transferring medication from the cartridge into a syringe with a needle. In this embodiment the coupling means for engaging the needle assembly may be replaced by coupling means for engaging the syringe, or coupling means for both may be provided. The coupling means may be a syringe holder, for example a cylinder coupled to the cartridge comprising a central bore for receiving the syringe. The syringe is coupled to the cartridge having the needle piercing the sealing. By activation of the dosing means the metered amount of medication is driven into the syringe. The syringe is then ready for injection after being removed from the cartridge.

Drawings

Fig. 1 is an exploded perspective view of the medication delivery device.

Fig. 2 is a cross-sectional view showing part of the medication delivery device, 2a immediately after assembling before the first injection, and 2b after some time of use.

Fig. 3 is a cross-sectional view showing the cartridge before assembling of the medication delivery device.

Detailed description of the invention

A medication delivery device in accordance with the present invention is identified generally by the numeral 20 in Fig. 1 and 2. Medication delivery device 20 includes a dosing assembly 6, and cartridge assembly 1, a needle assembly 16 and a cap 14.

The dosing assembly 6 is illustrated in Fig. 1 and 2. It is understood, however, that the dosing assembly 6 according to the invention may be any suitable dosing unit including plunger means; and accordingly, that variations from the depicted embodiment may be provided, and are considered to be within the scope of this invention. In the depicted embodiment the dosing assembly 6 includes a cylindrical housing surrounding the plunger means 17 of the dosing unit and having opposed proximal and distal ends.

In one aspect of the invention the plunger means comprises a rod element 7 which is adapted to engage the stopper 4 of the cartridge assembly 1. The rod element 7 advances axially into the cartridge 5 during injections. The dosing assembly may have any suitable driving means for advancing the rod element 7.

The dosing unit 6 preferably also comprises scale means 10 indicating the dosing quantity selected by activating the dose setting means 9 for defining specified selected doses of medication to be delivered. The selected dose may be delivered by actuating the actuator button 18. The actuator button is part of the driving means of the dosing assembly exerting its force on the rod element 7.

The dosing assembly further comprises coupling means 8 adapted for engagement with the cartridge assembly. The coupling means 8 may be internal or external couplings. In a preferred embodiment the coupling 8 is an internal coupling.

The cartridge assembly 1 is illustrated in Fig. 1 and 2, and in greater detail in Fig. 3. In Fig. 1 cartridge assembly 1 includes a moulded cartridge 5 extending from proximal end 21 to distal end 22.

At the distal end 22 of the cartridge assembly 1 is provided coupling means 2 for releasably mounting a needle assembly 11. At the proximal end 21 of the cartridge assembly 1 is provided coupling means 3 for mounting a dosing assembly 6. The coupling means are as described above.

Cartridge 5 also comprises a stopper 4 in sliding fluid tight engagement within said cartridge 5. The stopper 4 is adapted to receive the plunger means, such as a rod element 7 of the dosing assembly 6. The rod element 7 is adapted to exert an axial movement of the stopper 4 towards the sealed end 22 of the cartridge 5.

The cartridge assembly 1 may further comprise a housing for protecting some or all of the cartridge 5. When the cartridge assembly 1 includes a housing, one of the couplings 2, 3 of the cartridge may be moulded unitarily with the housing.

Instead of the protective housing the cartridge 5 may have integrally moulded reinforcements of the cartridge wall.

The depicted cartridge 5 is cylindrical having couplings 2, 3 at opposed ends. However, the cartridge may obtain any suitable form and the cross-section may be circular or non-circular, such as substantially triangular or oval.

The device according to the invention may include a protective cap 14 that is removably mounted over the cartridge assembly 1 and/or the needle 11 and which is removed before injection of the medication in the cartridge 5. The cap further ensures that the content of the cartridge is protected against sunlight.

Referring to Fig. 3 the coupling means of the cartridge are shown in greater detail. The coupling means 3 is an external thread, whereas the coupling means 2 is a recess for a snap lock of the needle assembly. Both coupling means are moulded unitarily with the cartridge.

The various parts of the medication delivery device are advantageously made of plastics, e.g. by injection moulding.

The medication delivery device 20 may further comprise any appropriate needle assembly 11, such as a double ended needle 13 having opposed proximal and distal points and a lumen extending axially therebetween.

A mounting hub 12 is engaged on the needle 13 and is removably connected to the coupling means 2 at the needle end of the cartridge assembly. The relative location of the mounting hub 12 ensures that the proximal point of the needle 13 will pierce the sealing when the mounting hub 12 is engaged with the coupling means 2 on the cartridge assembly 1.

The needle assembly 11 may further comprise a removable shield or cap 15 for protecting against accidental needle sticks.

The device according to the invention is suitable for delivering pre-set dosages of insulin, it is however understood that the device is suitable for the injection of pre-set dosages of other liquids.

In use the user will set the dose by means of the dose setting means 9. Before activating the actuator button 18 the cap 14 must be removed from the cartridge assembly 1 whereby the device 20 is prepared for an injection. The injection is effected by activating the actuator button 18, which again will cause ~~effect~~ the stopper 4 to be moved towards the sealed end 22 of the cartridge 5, thereby delivering the desired pre-set dosage. A subsequent dosage of medication will be set in exactly the same manner as described above. However, for such a subsequent dosage, the rod element 7 and the stopper 4 will be in a partly advanced position as starting point. Dose setting and injections can be carried out until all of the medication has been used.

Claims:

1. A medication delivery device comprising a cartridge assembly, a dosing assembly and optionally a needle assembly,

said cartridge assembly having one end sealed with a pierceable sealing, said end of the cartridge assembly comprising coupling means for engaging a needle assembly, and another end comprising coupling means for engaging the dosing assembly, said cartridge assembly further comprising a cartridge wherein at least one of the coupling means of said cartridge assembly is unitarily moulded with the cartridge, the cartridge further comprising a stopper adapted to receive plunger means, and

said dosing assembly comprising plunger means having coupling means for engaging the cartridge, and said plunger means is adapted to engage the stopper of the cartridge when the dosing assembly is coupled to the cartridge.

2. The medication delivery device according to claim 1, wherein all the coupling means of the cartridge assembly are unitarily moulded with the cartridge.

3. The medication delivery device according to claim 1, wherein at least one coupling means of the cartridge is an external coupling.

4. The medication delivery device according to claim 1, wherein at least one coupling means of the cartridge is a threaded coupling.

5. The medication delivery device according to claim 4, wherein the coupling means for engaging to dosing means is an external threaded coupling.

6. The medication delivery device according to claim 1, wherein the cartridge is moulded of a plastic material.

7. The medication delivery device according to claim 4, wherein the cartridge is at least partly transparent.

8. The medication delivery device according to claim 1, wherein reinforcements of the cartridge wall are integrally moulded with the cartridge.

9. The medication delivery device according to claim 1, wherein the cartridge further comprises a cartridge housing.

10. The medication delivery device according to claim 1, wherein the cartridge further comprise a scale.

11. The medication delivery device according to claim 1, wherein the cross-section of the cartridge is non-circular.

12. The medication delivery device according to claim 1, wherein the coupling means of the cartridge are opposed each other.

13. The cartridge assembly for use in a medication delivery device, said cartridge assembly having one end sealed with a pierceable sealing, said end of the cartridge assembly comprising coupling means for engaging a needle assembly, and another end comprising coupling means for engaging the dosing assembly, said cartridge assembly further comprising a cartridge wherein at least one of the coupling means of said cartridge assembly is unitarily moulded with the cartridge, said cartridge further comprising a stopper.

14. The cartridge assembly according to claim 13, wherein all the coupling means of the cartridge are unitarily moulded with the cartridge.

15. The cartridge assembly according to claim 13, wherein at least one coupling means of the cartridge is an external coupling.

16. The cartridge assembly according to claim 13, wherein at least one coupling means of the cartridge is a threaded coupling.

17. The cartridge assembly according to claim 16, wherein the coupling means for engaging to dosing means is an external threaded coupling.

18. A cartridge assembly according to claim 13, wherein the cartridge is moulded of a plastic material.

19. A cartridge assembly according to claim 13, wherein the cartridge is at least partly transparent.

20. A cartridge assembly according to claim 13, wherein reinforcements of the cartridge wall are integrally moulded with the cartridge.

21. A cartridge assembly according to claim 13, wherein the cartridge further comprises a cartridge housing.

22. A cartridge assembly according to claim 13, wherein the cartridge further comprise a scale.

23. A cartridge assembly according to claim 13, wherein the cross-section of the cartridge is non-circular.

24. A cartridge assembly according to claim 13, wherein the coupling means of the cartridge are opposed each other.

25. A cartridge assembly according to claim 13, which is filled with medicine.

Abstract

The present invention relates to a medication delivery device comprising a cartridge assembly, a dosing assembly and optionally a needle assembly. The cartridge assembly comprises a cartridge having a stopper adapted to receive a plunger means. Furthermore, the cartridge assembly has one end sealed with a pierceable sealing, said end comprising coupling means for engaging a needle assembly, and another end comprising coupling means for engaging the dosing assembly. At least one of the coupling means of the cartridge assembly is unitarily moulded with the cartridge. The dosing assembly comprises a plunger means and has coupling means for engaging the cartridge assembly. The cartridge assembly and the dosing assembly are coupled together for delivering selected doses of medication. The cartridge is preferably moulded from a plastic material, such as a transparent material, and may be housed in a cartridge housing for protection of the cartridge. The coupling means may be selected from threaded locks, snap locks, hinged locks, or bajonet locks. The medication delivery device is especially suitable for delivering insulin, growth hormone or ~~the like~~ other medicines.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to PCT International Applications)

Docket Number: 200-US

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Medication Delivery Device

the specification of which (check only one item below):

[ ] is attached hereto

[X] was filed as United States application

Application No. to be assigned

on July 7, 1999

and was amended

on _____

[ ] was filed as PCT international application

Number _____

on _____

and was amended under PCT Article 19

on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim priority benefits under Title 35, United States Code, §119 of any provisional or foreign applications(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign applications(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR U.S. PROVISONAL/FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
Denmark	PA 1998 00909	July 8, 1998	[X] YES [ ] NO
Denmark	PA 1998 01500	November 17, 1998	[X] YES [ ] NO
USA	60/098,702	September 1, 1998	[X] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO

PTO 1391 (REV. 10-83)

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to PCT International Applications)

Attorney's Docket Number: S[illegible]200-US

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this applications is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS (Check one)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	Patented	Pending	Abandoned

PCT APPLICATIONS DESIGNATING THE U.S.

APPLICATION NO.	FILING DATE	US SERIAL NUMBERS ASSIGNED (if any)			

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COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Includes Reference to PCT International Applications)				Attorney Docket Number: 5[illegible].200-US
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7	Full Name of Inventor	Family Name:	First Given Name:	Second Given Name:
	Residence & Citizenship	City:	State or Foreign Country:	Country of Citizenship:
	Post Office Address	Post Office Address:	City:	State & Zip Code/Country:
8	Full Name of Inventor	Family Name:	First Given Name:	Second Given Name:
	Residence & Citizenship	City:	State or Foreign Country:	Country of Citizenship:
	Post Office Address	Post Office Address:	City:	State & Zip Code/Country:
	Full Name of Inventor	Family Name:	First Given Name:	Second Given Name:
	Residence & Citizenship	City:	State or Foreign Country:	Country of Citizenship:
	Post Office Address	Post Office Address:	City:	State & Zip Code/Country:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signature of Inventor 1	Signature of Inventor 2	Signature of Inventor 3
Date	Date	Date
Signature of Inventor 4	Signature of Inventor 5	Signature of Inventor 6
Date	Date	Date
Signature of Inventor 7	Signature of Inventor 8	Signature of Inventor 9
Date	Date	Date

1/2

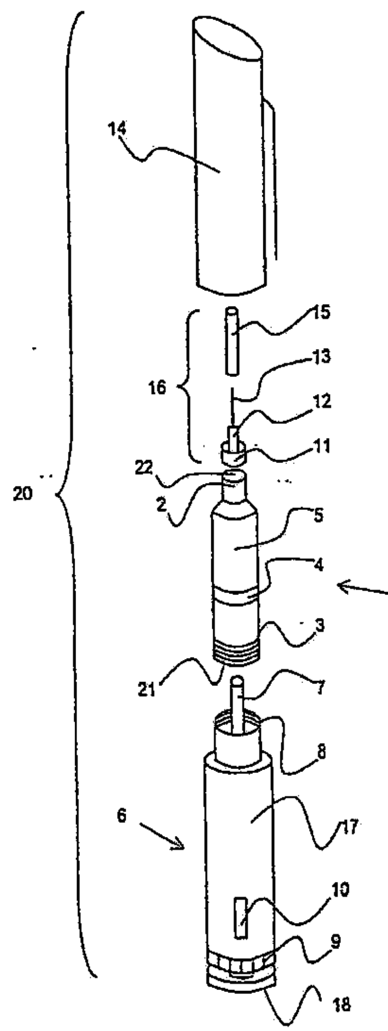

Fig. 1

PRINT OF DRAWINGS
AS ORIGINALLY FILED

2/2

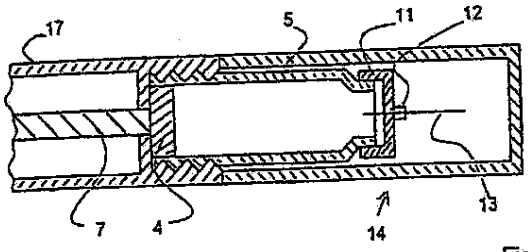

Fig. 2 a

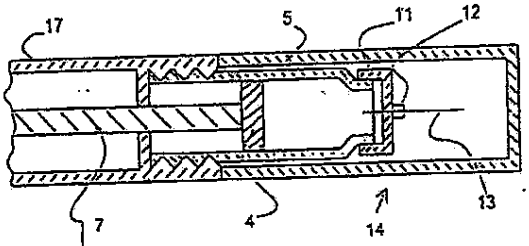

Fig. 2 b

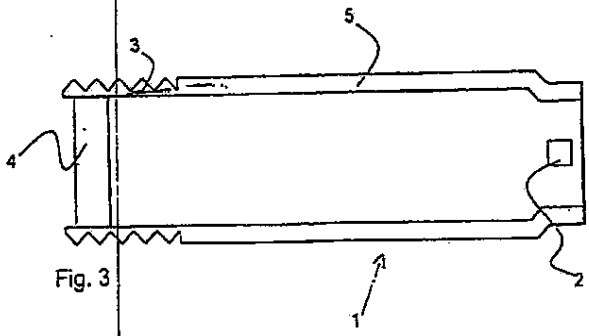

Fig. 3

PRINT OF DRAWINGS
AS ORIGINALLY FILED

1 / 2

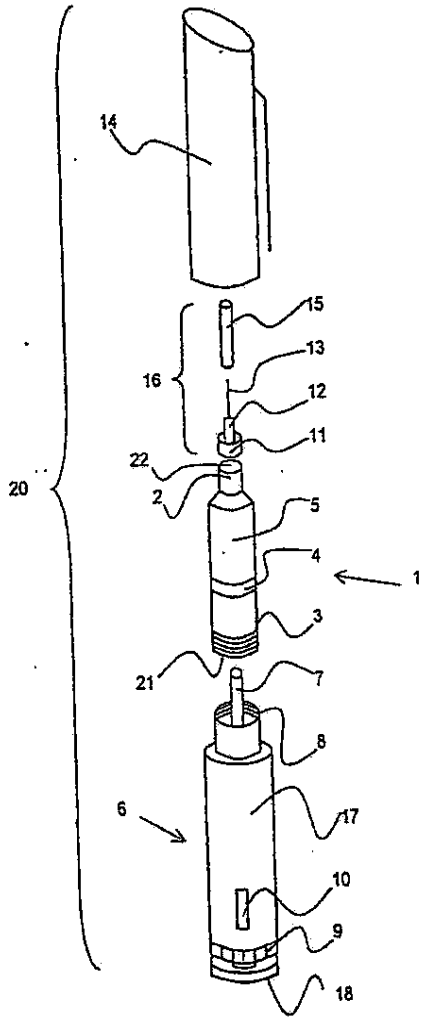

Fig. 1

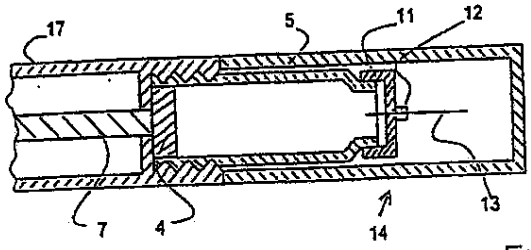

Fig. 2 a

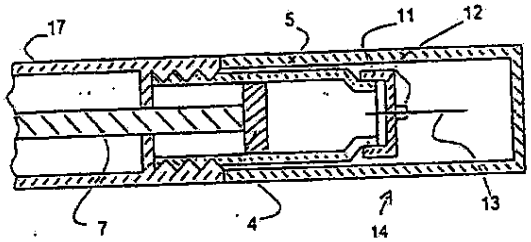

Fig. 2 b

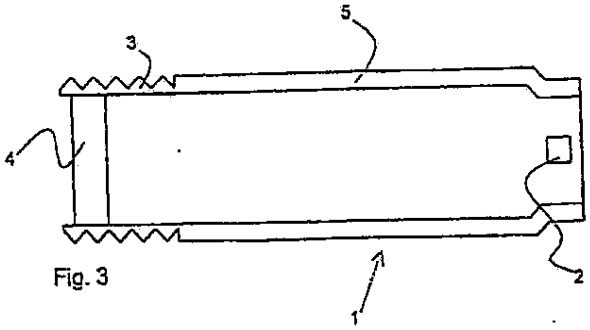

Fig. 3

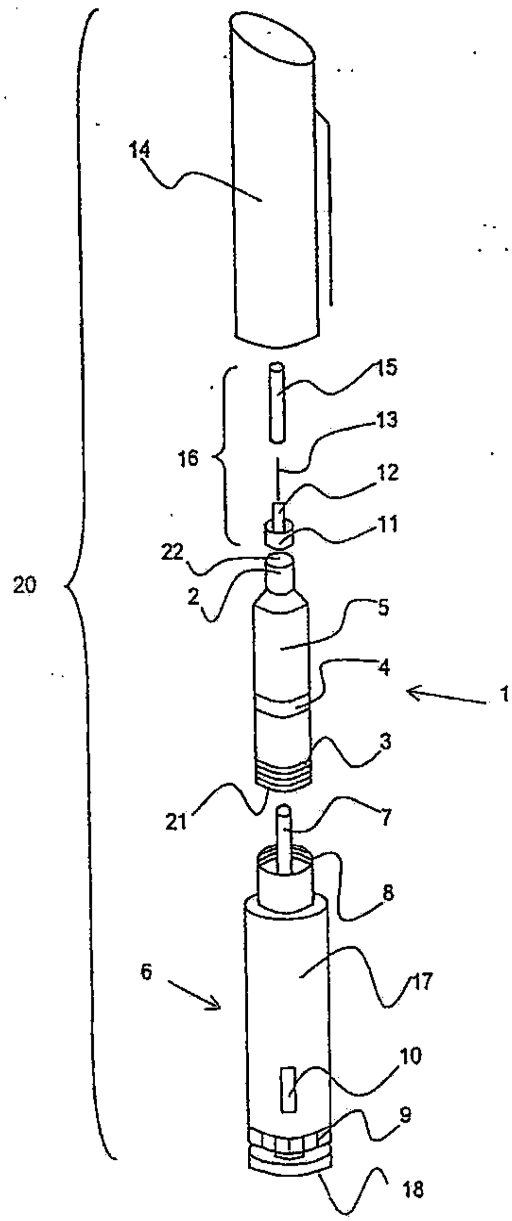

Fig. 1

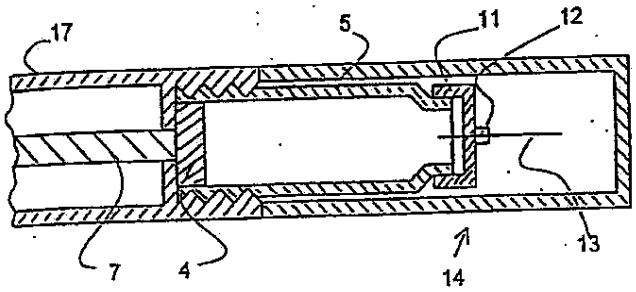

Fig. 2 a

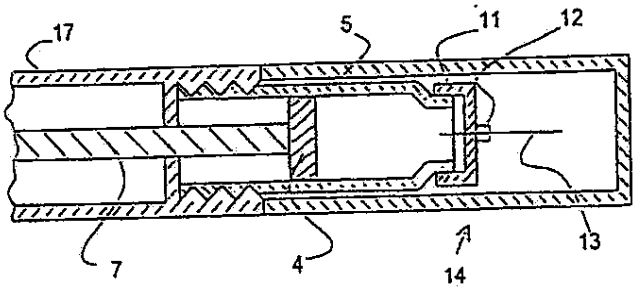

Fig. 2 b

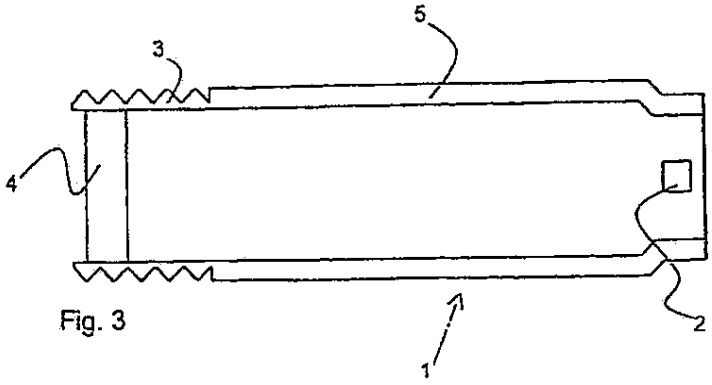

Fig. 3

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1/2

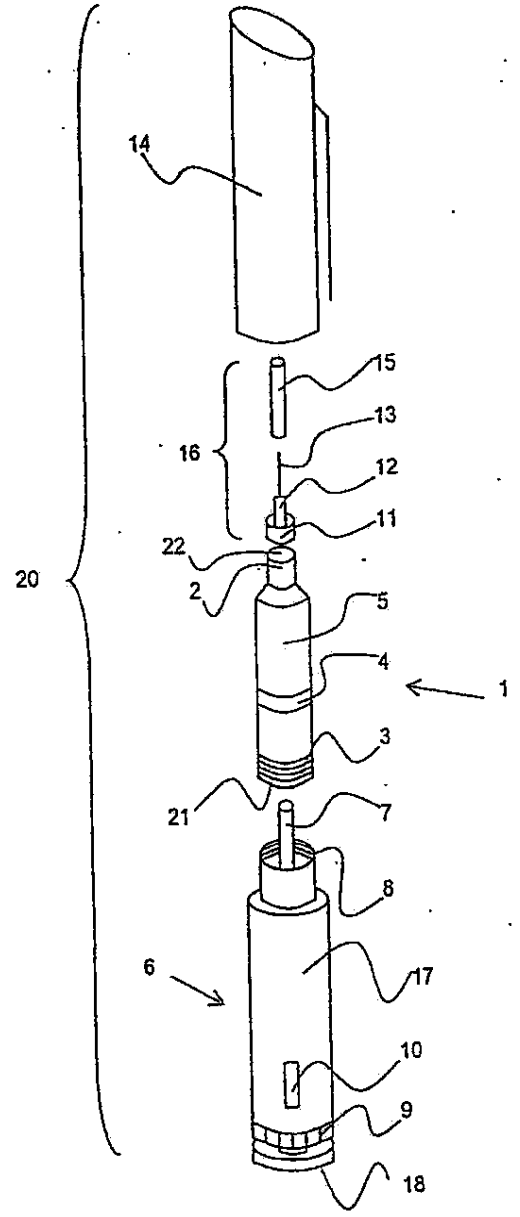

Fig. 1

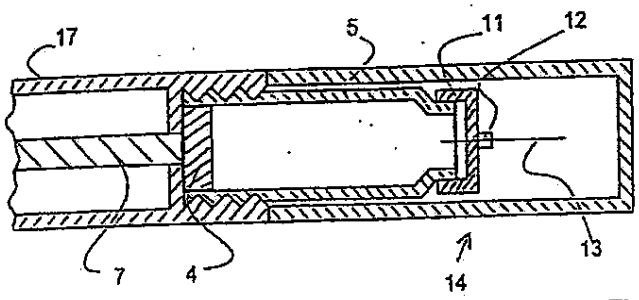

Fig. 2 a

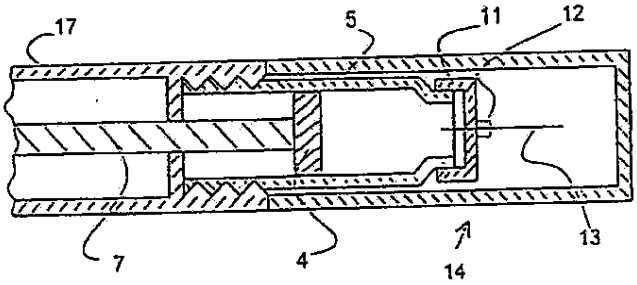

Fig. 2 b

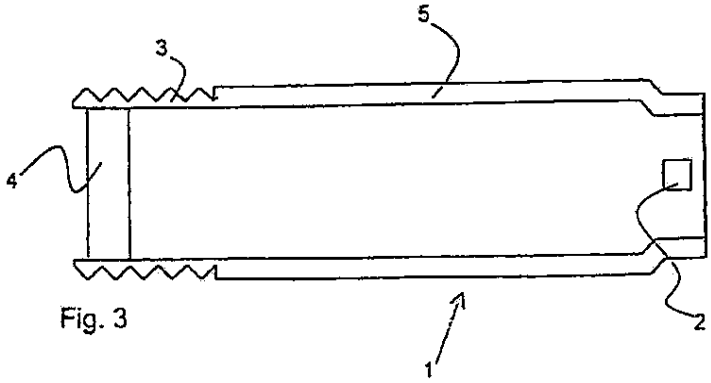

Fig. 3

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO./TITLE
09/348,536	07/07/99	BUCH-RASMUSSEN	T 5637.200-US

0242/0805

STEVE T ZELSON ESQ
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE SUITE 6400
NEW YORK NY 10174-6401

NOT ASSIGNED

3734

DATE MAILED: 08/05/99

NOTICE TO FILE MISSING PARTS OF APPLICATION
Filing Date Granted

An Application Number and Filing Date have been assigned to this application. The items indicated below, however, are missing. Applicant is given TWO MONTHS FROM THE DATE OF THIS NOTICE within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). If any of items 1 or 3 through 5 are indicated as missing, the SURCHARGE set forth in 37 CFR 1.16(e) of ☐ $65.00 for a small entity in compliance with 37 CFR 1.27, or ☐ $130.00 for a non-small entity, must also be timely submitted in reply to this NOTICE to avoid abandonment.

If all required items on this form are filed within the period set above, the total amount owed by applicant as a ☐ small entity (statement filed) ☐ non-small entity is $ 130.00.

☐ 1. The statutory basic filing fee is:
- ☐ missing.
- ☐ insufficient.

Applicant must submit $_____ to complete the basic filing fee and/or file a small entity statement claiming such status (37 CFR 1.27).

☐ 2. The following additional claims fees are due:

$_____ for _____ total claims over 20.

$_____ for _____ independent claims over 3.

$_____ for multiple dependent claim surcharge.

Applicant must either submit the additional claim fees or cancel additional claims for which fees are due.

☑ 3. The oath or declaration:
- ☑ is missing or unsigned.
- ☐ does not cover the newly submitted items.

An oath or declaration in compliance with 37 CFR 1.63, including residence information and identifying the application by the above Application Number and Filing Date is required.

☐ 4. The signature(s) to the oath or declaration is/are by a person other than inventor or person qualified under 37 CFR 1.42, 1.43 or 1.47.
A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Application Number and Filing Date, is required.

☐ 5. The signature of the following joint inventor(s) is missing from the oath or declaration:

_____

An oath or declaration in compliance with 37 CFR 1.63 listing the names of all inventors and signed by the omitted inventor(s), identifying this application by the above Application Number and Filing Date, is required.

☐ 6. **A $50.00 processing fee is required since your check was returned without payment (37 CFR 1.21(m)).**

☐ 7. Your filing receipt was mailed in error because your check was returned without payment.

☐ 8. The application was filed in a language other than English.
Applicant must file a verified English translation of the application, the $130.00 set forth in 37 CFR 1.17(k), unless previously submitted, and a statement that the translation is accurate (37 CFR 1.52(d)).

☐ 9. OTHER: _____

Direct the reply and any questions about this notice to "Attention: Box Missing Parts."

A copy of this notice MUST be returned with the reply.

Regina Fields
Customer Service Center
Initial Patent Examination Division (703) 308-1202

FORM PTO-1533 (REV. 9/98)

U.S. GPO: 1998-445-824

PART 3 - OFFICE COPY

OIPE JC35 OCT 12 1999 PATENT & TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

#3

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO./TITLE
09/348,536	07/07/99	BUCH-RASMUSSEN	T 5637.200-US

0242/0805

STEVE T ZELSON ESQ
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE SUITE 6400
NEW YORK NY 10174-6401

NOT ASSIGNED

3734

DATE MAILED: 08/05/99

NOTICE TO FILE MISSING PARTS OF APPLICATION
Filing Date Granted

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All required items on this form are filed within the period set above, the total amount owed by applicant as a small entity (statement filed) ☐ non-small entity is $ 130.00.

1. The statutory basic filing fee is:
   - ☐ missing.
   - ☐ insufficient.

   Applicant must submit $_____ to complete the basic filing fee and/or file a small entity statement claiming such status (37 CFR 1.27).
2. ☐ The following additional claims fees are due:

   $_____ for _____ total claims over 20.

   $_____ for _____ independent claims over 3.

   $_____ for multiple dependent claim surcharge.

   Applicant must either submit the additional claim fees or cancel additional claims for which fees are due.
3. ☑ The oath or declaration:
   - ☑ is missing or unsigned.
   - ☐ does not cover the newly submitted items.

   An oath or declaration in compliance with 37 CFR 1.63, including residence information and identifying the application by the above Application Number and Filing Date is required.
4. ☐ The signature(s) to the oath or declaration is/are by a person other than inventor or person qualified under 37 CFR 1.42, 1.43 or 1.47.

   A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Application Number and Filing Date, is required.
5. ☐ The signature of the following joint inventor(s) is missing from the oath or declaration:

   _____

   An oath or declaration in compliance with 37 CFR 1.63 listing the names of all inventors and signed by the omitted inventor(s), identifying this application by the above Application Number and Filing Date, is required.
6. ☐ A $50.00 processing fee is required since your check was returned without payment (37 CFR 1.21(m)).
7. ☐ Your filing receipt was mailed in error because your check was returned without payment.
8. ☐ The application was filed in a language other than English.

   Applicant must file a verified English translation of the application, the $130.00 set forth in 37 CFR 1.17(k), unless previously submitted, and a statement that the translation is accurate (37 CFR 1.52(d)).
9. ☐ OTHER: _____

Direct the reply and any questions about this notice to "Attention: Box Missing Parts."

A copy of this notice MUST be returned with the reply.

Regina Fields
Customer Service Center
Initial Patent Examination Division (703) 308-1202

FORM PTO-1533 (REV. 9/98)

U.S. GPO: 1998-[illegible]

PART 2 - COPY TO BE RETURNED WITH RESPONSE

09348536 141447 00000034 130.00 CH
10/14/1999 TLUU11 01 FC:105

COMBINED DECLARATION FOR PA[illegible] APPLICATION AND POWER OF ATTORN[illegible]
(Includes Reference to PCT International Applications)

Attorney's Docket Number: 5637.200-US

#3

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Medication Delivery Device

the specification of which (check only one item below):

[ ] is attached hereto

[X] was filed as United States application

Application No. to be assigned

on July 7, 1999

and was amended

on _____

[ ] was filed as PCT international application

Number _____

on _____

and was amended under PCT Article 19

on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim priority benefits under Title 35, United States Code, §119 of any provisional or foreign applications(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign applications(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR U.S. PROVISONAL/FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
Denmark	PA 1998 00909	July 8, 1998	[X] YES [ ] NO
Denmark	PA 1998 01500	November 17, 1998	[X] YES [ ] NO
USA	60/098,702	September 1, 1998	[X] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO

COMBINED DECLARATION FOR PA[illegible] APPLICATION AND POWER OF ATTORN[illegible]
(Includes Reference to PCT International Applications)

Attorney's Docket Number: 3637.200-US

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this applications is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS (Check one)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	Patented	Pending	Abandoned

PCT APPLICATIONS DESIGNATING THE U.S.

APPLICATION NO.	FILING DATE	US SERIAL NUMBERS ASSIGNED (if any)			

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

Steve T. Zelson Reg. No. 30,335 | Elias J. Lambiris Reg. No. 33,728 | Valeta A. Gregg Reg. No. 35,127 | Carol B. Rozek Reg. No. 36,993 | Robert L. Starnes Reg. No. 41,324 | Reza Green Reg. No. 38,475

Send Correspondence to: Steve T. Zelson, Esq.
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, New York 10174-6400

Direct Telephone Calls To:
Steve T. Zelson
(212) 867-0123

		Family Name	First Given Name	Second Given Name
1	Full Name of Inventor	Buch-Rasmussen	Thomas	
	Residence & Citizenship	City: DK-2820 Gentofte	State or Foreign Country: Denmark	Country of Citizenship: Denmark
	Post Office Address	Post Office Address: Dalvej 28	City: DK-2820 Gentofte	State & Zip Code/Country: Denmark
2	Full Name of Inventor	Munk	Benny	
	Residence & Citizenship	City: DK-2650 Hvidorre	State or Foreign Country: Denmark	Country of Citizenship: Denmark
	Post Office Address	Post Office Address: Bjæverskov Allé 52	City: DK-2720 Vanløse	State & Zip Code/Country: Denmark
3	Full Name of Inventor	Poulsen	Jens	Ulrik
	Residence & Citizenship	City: DK-2830 Virum	State or Foreign Country: Denmark	Country of Citizenship: Denmark
	Post Office Address	Post Office Address: Virumgade 54 C	City: DK-2830 Virum	State & Zip Code/Country: Denmark
4	Full Name of Inventor	Ljungreen	Henrik	
	Residence & Citizenship	City: DK-2750 Ballerup	State or Foreign Country: Denmark	Country of Citizenship: Denmark
	Post Office Address	Post Office Address: Jonstrupvej 244A	City: DK-2750 Ballerup	State & Zip Code/Country: Denmark

COMBINED DECLARATION FOR PA[illegible] APPLICATION AND POWER OF ATTORN[illegible] Attorney's Docket Number: 5637.200-US
(Includes Reference to PCT International Applications)

5	Full Name of Inventor	Family Name: Jensen	First Given Name: Peter	Second Given Name: Møller
	Residence & Citizenship	City: D-2970 Hørsholm	State or Foreign Country: Denmark	Country of Citizenship: Denmark
	Post Office Address	Post Office Address: Svenstrupvej 6	City: D-2970 Hørsholm	State & Zip Code/Country: Denmark
6	Full Name of Inventor	Family Name: Jensen	First Given Name: Jens	Second Given Name: Møller
	Residence & Citizenship	City: DK-1051 Copenhagen K	State or Foreign Country: Denmark	Country of Citizenship: Denmark
	Post Office Address	Post Office Address: Nyhavn 37	City: DK-1051 Copenhagen K	State & Zip Code/Country: Denmark
7	Full Name of Inventor	Family Name:	First Given Name:	Second Given Name:
	Residence & Citizenship	City:	State or Foreign Country:	Country of Citizenship:
	Post Office Address	Post Office Address:	City:	State & Zip Code/Country:
8	Full Name of Inventor	Family Name:	First Given Name:	Second Given Name:
	Residence & Citizenship	City:	State or Foreign Country:	Country of Citizenship:
	Post Office Address	Post Office Address:	City:	State & Zip Code/Country:
9	Full Name of Inventor	Family Name:	First Given Name:	Second Given Name:
	Residence & Citizenship	City:	State or Foreign Country:	Country of Citizenship:
	Post Office Address	Post Office Address:	City:	State & Zip Code/Country:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signature of Inventor 5	Signature of Inventor 6	Signature of Inventor 7
Date: 2/8-99	Date: 16/8-99	Date: 5-8-99
Signature of Inventor 8	Signature of Inventor 9	Signature of Inventor 10
Date: 18/8-99	Date: 23/8-99	Date
Signature of Inventor 11	Signature of Inventor 12	Signature of Inventor 13
Date	Date	Date

Attorney Docket No.: 5637.200-US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Rasmussen et al.

Serial No.: 09/348,536 Group Art Unit: 3734

Filed: July 7, 1999 Examiner: TBA

For: Medication Delivery Device

CERTIFICATE OF MAILING UNDER 37 CFR 1.8(a)

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

I hereby certify that the attached correspondence comprising:

1. Response to Notice to File Missing Parts (in duplicate)
2. Copy of Notice to File Missing Parts
3. Executed Combined Declaration and Power of Attorney

is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

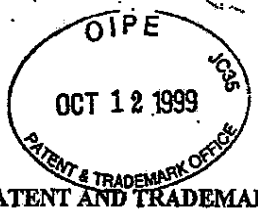
Commissioner of Patents and Trademarks
Washington, DC 20231

on October 5, 1999.

Miriam Kelly

(signature of person mailing paper)

Attorney Docket No.: 5637.200-US



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Rasmussen et al.

Serial No.: 09/348,536 Group Art Unit: 3734

Filed: July 7, 1999 Examiner: TBA

For: Medication Delivery Device

RESPONSE TO NOTICE TO FILE MISSING PARTS

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

In response to the Notice to File Missing Parts dated August 5, 1999 (a copy thereof is attached hereto), Applicants submit the Combined Declaration and Power of Attorney signed and dated by Applicants for the above-captioned application.

Please charge the required fee, estimated to be $130.00, to Novo Nordisk of North America, Inc., Deposit Account No. 14-1447. Please credit any overpayment to Deposit Account No. 14-1447. A duplicate of this sheet is enclosed.

Respectfully submitted,

Date: October 5, 1999

Carol E. Rozek

Carol E. Rozek, Reg. No. 36,993
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123

Attorney Docket No.: 5637.200-US PATENT

#41 hel

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FILING UNDER 37 C.F.R. 1.53(b)

Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

Express Mail Label No. EL293688877US
Date of Deposit July 7, 1999

Sir:

This is a request for filing an application under 37 C.F.R. 1.53(b) of

Applicant(s): Buch-Rasmussen et al.

Title: Medication Delivery Device

13 pages of specification 2 sheets of formal drawings

3 sheets of Declaration and Power of Attorney

[x] The filing fee is calculated as follows:

Basic Fee:	$ 760.00
Total Claims: 25 - 20 = 5 x 18 =	$ 90.00
Independent Claims: 2 - 3 = 0 x 78 =	$ 0.00
Total Fee:	$ 850.00

Priority of Danish application nos. PA 1998 00909 filed on July 8, 1998 and PA 1998 01500 filed on November 17, 1998 are claimed under 35 U.S.C. 119. Certified copies are submitted herewith.

Priority of U.S. provisional application no. 60/098,702 filed on September 1, 1998 are claimed under 35 U.S.C. 119.

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority under 35 U.S.C. 119 of Danish application serial nos. PA 1998 00909 filed July 8, 1998, PA 1998 01500 filed November 17, 1998, and U.S. Provisonal application serial no. 60/098,702 filed September 1, 1998, the contents of which are fully incorporated herein by reference.

Address all future communications to Steve T. Zelson, Esq., Novo Nordisk of North America, Inc., 405 Lexington Avenue, Suite 6400, New York, NY 10174-6401.

Please charge the required fee, estimated to be $850, to Novo Nordisk of North America, Inc., Deposit Account No. 14-1447. A duplicate of this sheet is enclosed.

Respectfully submitted,

Date: July 7, 1999

Carol E. Rozek

Carol E. Rozek, Reg. No. 36,993
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123

09348536 . 070799

Attorney Docket No.: 5637.200-US. PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Rasmussen et al.

Application No.: TBA Group Art Unit: TBA

Filed: July 7, 1999 Examiner: TBA

For: Medication Delivery Device

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Before the above-captioned application is taken up for examination, entry of the following amendment is respectfully requested:

IN THE SPECIFICATION:

At page 1, before the first line, insert the title: –Medication Delivery Device–.

At page 1, after the title, insert:

–CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority under 35 U.S.C. 119 of Danish application nos. PA 1998 00909 filed July 8, 1998 and PA 1998 01500 filed November 17, 1998, and U.S. provisional application no. 60/098,702 filed September 1, 1998, the contents of which are fully incorporated herein by reference.–

IN THE CLAIMS:

Claim 2, line 1, first word, change "A" to –The–.

Claim 3, line 1, first word, change "A" to –The–.

Claim 4, line 1, first word, change "A" to --The--.

Claim 5, line 1, first word, change "A" to --The--.

Claim 6, line 1, first word, change "A" to --The--.

Claim 7, line 1, first word, change "A" to --The--.

Claim 8, line 1, first word, change "A" to --The--.

Claim 9, line 1, first word, change "A" to --The--.

Claim 10, line 1, first word, change "A" to --The--.

Claim 11, line 1, first word, change "A" to --The--.

Claim 12, line 1, first word, change "A" to --The--.

Claim 14, line 1, first word, change "A" to --The--.

Claim 15, line 1, first word, change "A" to --The--.

Claim 16, line 1, first word, change "A" to --The--.

Claim 17, line 1, first word, change "A" to --The--.

Claim 18, line 1, first word, change "A" to --The--.

Claim 19, line 1, first word, change "A" to --The--.

Claim 20, line 1, first word, change "A" to --The--.

Claim 21, line 1, first word, change "A" to --The--.

Claim 22, line 1, first word, change "A" to --The--.

Claim 23, line 1, first word, change "A" to --The--.

Claim 24, line 1, first word, change "A" to --The--.

Claim 25, line 1, first word, change "A" to --The--.

REMARKS

This amendment is submitted solely to correct the article "A" to "The" in the dependent claims. Since no new matter was been introduced by this amendment, entry of the amendment is respectfully requested.

Respectfully submitted,

Date: July 7, 1999

Carol E. Rozek, Reg. No. 36,993
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/348,536	07/07/99	BUCH-RASMUSSEN	T 5637.200-US

QM12/0309

STEVE T ZELSON ESQ
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE SUITE 6400
NEW YORK NY 10174-6401

EXAMINER	
SIRMONS, K	
ART UNIT	PAPER NUMBER
3763	6

DATE MAILED: 03/09/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95) 1- File Copy

Office Action Summary	Application No. 09/348,536	Applicant(s) Thomas Bush-Rasmussen et al
	Examiner Kevin C. Sirmons	Group Art Unit 3763

☒ Responsive to communication(s) filed on *Jul 7, 1999*

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *1* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-25* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-25* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-12 are, drawn to medication device, classified in class 604, subclass 232.

   II. Claims 13-25 are, drawn to a cartridge assembly, classified in class 604, subclass 232.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as mutually exclusive species in an intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product (MPEP § 806.04(b), 3rd paragraph), and the species are patentably distinct (MPEP § 806.04(h)). In the instant case, the intermediate product is deemed to be useful as a valve and the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. A telephone call was made to Carol E. Rozek on 2/2/00 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Kevin C. Sirmons whose telephone number is (703)306-5410. The examiner can normally be reached on Monday - Thursday from 6:30 am to 4:00 pm. The examiner can also be reached on alternate Fridays.

If attempt to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wynn Wood Coggins, can be reached on (703) 308-1344.

/CCS

Kevin C. Sirmons

Patent Examiner

2/2/00

WYNN WOOD COGGINS
SUPERVISORY PATENT EXAMINER

Attorney Docket No.: 5637.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Buch-Rasmussen et al.

Serial No.: 09/348,536 Group Art Unit: 3763

Filed: July 7, 1999 Examiner: K. Sirmons

For: Medication Delivery Device

CERTIFICATE OF FACSIMILE TRANSMISSION

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

I hereby certify that the attached correspondence comprising:

1. Response to Restriction Requirement

was sent to the United States Patent Office by telefax to the attention of Examiner K. Sirmons, fax number (703) 305-3704.

Respectfully submitted,

Date: April 4, 2000

Miriam Kelly
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123

Attorney Docket No.: 5637.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Buch-Rasmussen et al.

Application No.: 09/348,538 Group Art Unit: 3763

Filed: July 7, 1999 Examiner: K. Simmons

For: Medication Delivery Device

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

This paper is being filed in response to the Office Action mailed March 9, 2000 wherein the Examiner requested Applicants to elect one of two (2) designated groups.

In response to this requirement, Applicants hereby elect with traverse the invention of Group I (claims 1-12), drawn to a medication device. Applicants hereby reserve the right to file a continuing application directed to the nonelected subject matter.

The basis for traverse is that there would not be a serious burden on the examiner if restriction were not required. Each of the two designated inventions is classified in Class 604, subclass 232.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this response or application.

Respectfully submitted,

Date: April 4, 2000

Carol E. Rozek

Carol E. Rozek, Reg. No. 36,993
Novo Nordisk of North America, Inc.
405 Lexington Avenue, Suite 6400
New York, NY 10174-6401
(212) 867-0123

APR. 4.2000 10:11AM NNNA NO.957 P.1/3

RESTRICTION ELECTION FACSIMILE TRANSMISSION

FAX RECEIVED
APR 4 2000
GROUP 1600

DATE: April 4, 2000

FROM/ATTORNEY: Carol Rozek, Esq.

FIRM: Novo Nordisk of No. America

PAGES, INCLUDING COVERSHEET: 3

PHONE NUMBER: (212) 878-9648

RECEIVED APR -6 2000 TC 2800 MAIL ROOM
RECEIVED APR -7 2000 TECH CENTER 3700

TO EXAMINER: K. Simmons, GAU 3763

SERIAL NUMBER: 09/348,636

FAX/TELECOPIER NUMBER: (703) 305-3704

PLEASE NOTE: THIS FACSIMILE NUMBER IS TO BE USED ONLY FOR RESPONSES TO RESTRICTIONS.

COMMENTS: See Attached.

IF YOU HAVE NOT RECEIVED ALL THE PAGES OF THIS TRANSMISSION, PLEASE CONTACT THE ATTORNEY AT THE TELEPHONE NUMBER LISTED ABOVE.

IN COMPLIANCE WITH 1096 OG 30, THE FILING DATE ACCORDED EACH OFFICIAL FAX TRANSMISSION WILL BE DETERMINED BY THE FAX MACHINE DATE STAMP FOUND ON THE LAST PAGE OF THE TRANSMISSION, UNLESS THAT DATE IS A SATURDAY, SUNDAY, OR FEDERAL HOLIDAY WITHIN THE DISTRICT OF COLUMBIA, IN WHICH CASE THE OFFICIAL DATE OF RECEIPT WILL BE THE NEXT BUSINESS DAY.

C:\donl\pwg\Fax_Flat

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/348,536	07/07/99	BUCH-RASMUSSEN	T 5637.200-US

QM32/0426

STEVE T ZELSON ESQ
NOVO NORDISK OF NORTH AMERICA INC
405 LEXINGTON AVENUE SUITE 6400
NEW YORK NY 10174-6401

EXAMINER	
SIRMONS,K	
ART UNIT	PAPER NUMBER
3763	8

DATE MAILED: 04/26/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/348,536	Thomas Bush-Rasmussen et al
Examiner	**Group Art Unit**
Kevin C. Simmons	3763

☒ Responsive to communication(s) filed on *Jul 7, 1999*

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-25* is/are pending in the applicat

Of the above, claim(s) *13-25* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that there would not be a serious burden on the examiner if restriction were not required. This is not found persuasive because group one also requires a search in 604/ 200, 201, 228, and 232-234. Furthermore, the search required for group one is not required for group II. In addition, group II is deemed useful as a valve and the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the reinforcements, a cartridge housing, and a cross-section of the cartridge that is non-circular must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 1, it is unclear if the applicant is claiming a needle assembly.

5. Claim 8 recites the limitation "reinforcements", "the cartridge wall", and claim 11 recites the limitation "the cross-section." There is insufficient antecedent basis for this limitation in the claim.

As to claim 9, it is unclear what the applicant considers the cartridge housing.

As to claim 11, it is unclear what the applicant considers to be the cross-section of the cartridge because it appears to be circular.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-9, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Reynolds US Pat. No. 5,364,369.

Reynolds discloses a medication delivery device comprising: a cartridge assembly (6), a dosing assembly (B) and optionally a needle assembly (2); said cartridge assembly having one end sealed with a pierceable sealing (5), said end of the cartridge assembly comprising coupling means for engaging a needle assembly (cartridge assembly engages the needle assembly forming a coupling means), and another end comprising coupling means for engaging the dosing assembly (18); said cartridge assembly further comprising a cartridge (6), wherein at least one of the coupling means of said cartridge assembly is unitarily moulded with the cartridge (4 and 5 are also considered by the examiner to be moulded coupling means with the cartridge), the cartridge further comprising a stopper (8) adapted to receive plunger means (10 and/or 14, it is the examiner's position that 10 and/or 14 are considered plunger means), and said dosing assembly comprising plunger means having coupling means for engaging the cartridge (note: (8) is a part of the cartridge (6), therefore, (10/14) which are considered the plunger means engages the cartridge (6)), and said plunger means is adapted to engage the stopper of the cartridge when the dosing assembly is coupled to the cartridge (figs. 1 and 2); wherein all the coupling means of the cartridge assembly are unitarily moulded with the cartridge (note:(8) is a part of the cartridge (6) which is considered one part, therefore, they are moulded; wherein at least one coupling means of the cartridge is an external coupling (4 and 5); wherein at least one coupling means of the cartridge is a threaded coupling (18); wherein the coupling means for engaging to dosing means is an external threaded coupling (8); wherein the cartridge is moulded of a plastic material (col. 10, lines 43-58); wherein the cartridge is at least partly transparent (col. 10, lines 43-58);

wherein reinforcements of the cartridge wall are integrally moulded with the cartridge (7, col. 2, lines 49-61); wherein the cartridge further comprises a cartridge housing (6); wherein the coupling means of the cartridge are opposed each other (figs. 1 and 2).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reynolds U.S. Pat. No. 5,364,369 in view of Sams U.S. Pat. No. 4,865,591.

Reynolds discloses a medication delivery device substantially as claimed except for: wherein the cartridge further comprise a scale. However, Sams discloses a cartridge with a scale. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the cartridge of Reynolds using the scale as taught by Sams, since Sams discloses that the scale will indicate to the user the amount of dosage selected for injection.

Conclusion

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Kevin C. Sirmons whose telephone number is (703)306-5410.

The examiner can normally be reached on Monday - Thursday from 6:30 am to 4:00 pm. The examiner can also be reached on alternate Fridays.

If attempt to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wynn Wood Coggins, can be reached on (703) 308-1344.

KCS

Kevin C. Sirmons

Patent Examiner

4/21/00

WYNN WOOD COGGINS
SUPERVISORY PATENT EXAMINER

FORM PTO-892	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NO.	
NOTICE OF REFERENCES CITED		09348536	3763		8
		APPLICANT(S) Bucj-Rasmussen			

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	A	5,364,369	11/1994	Reynolds	604	187	
	B	4,865,591	9/1989	Sams	604	186	
	C	5,554,125	9/1996	Reynolds	604	187	
	D	5,137,511	8/1992	Reynolds	604	88	
	E	4,597,753	7/1986	Turley	604	61	
	F						
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS
	L						
	M						
	N						
	O						
	P						
	Q						

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

	R	
	S	
	T	
	U	

EXAMINER	DATE	
Kevin C. Sirmons	April 21, 2000	Form892ccs2106b

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05(a).)

US005364369A

United States Patent [19]

Reynolds

[11] Patent Number: 5,364,369

[45] Date of Patent: Nov. 15, 1994

[54] SYRINGE

[76] Inventor: David L. Reynolds, 305 Knowlton Road, P.O. Box 600, (Knowlton) Lac Brome, Quebec, Canada, J0E 1V0

[21] Appl. No.: 791,399

[22] Filed: Nov. 14, 1991

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 437,203, Nov. 16, 1989, Pat. No. 5,137,511, which is a continuation-in-part of Ser. No. 72,015, Jul. 8, 1987, Pat. No. 4,886,495.

[30] Foreign Application Priority Data

Nov. 14, 1990 [GB] United Kingdom 9024710.7

[51] Int. Cl.[5] A61M 5/00

[52] U.S. Cl. 604/187; 604/88; 604/191; 604/416

[58] Field of Search 604/82, 87, 88, 89, 604/91, 92, 191, 187, 200, 201, 203-205, 411, 413-416, 905; 206/222; 215/247

[56] References Cited

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(List continued on next page.)

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Catalog Page Showing 'Uroject', Puls-A-Jet and 'Mini--Mix' Systems (date unknown).

'Vetter Lyo-Ject' Brochure, Vetter, 1985.

'The Syringe-Phial "Speed"', Sterimedical Supplies S.R.L. (date unknown).

'Kimble Glass Capabilities', Brochure (date unknown).

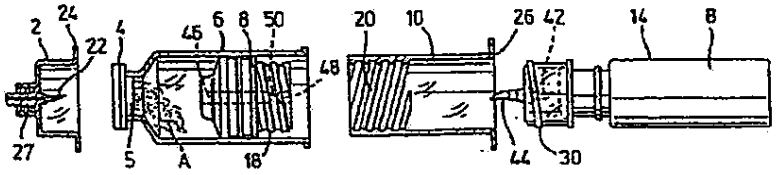
'West Capabilities . . . Glass Products' Brochure (date unknown).

Primary Examiner—Ralph A. Lewis
Attorney, Agent, or Firm—Ridout & Maybee

[57] ABSTRACT

A prefilled syringe for one or two component medicaments is based upon the use of a vial containing a medicament or one component of a medicament, the vial having an open bottom closed by a piston. When a flexible extension of the piston is coupled with a tubular plunger, and an adaptor cap having an internal needle and an external connection for a needle is placed over a cap of the vial, the latter is converted into a prefilled syringe. The piston may have an axial passage closed by a resealable septum, so that a separate diluent stored in a flexible capsule may be introduced into the vial through the piston by a double ended needle mounted on a further cap applied to the capsule, the further cap being coupled within the tubular interior of the plunger so that the double ended needle penetrates the septum in the piston. The capsule is pushed forward onto the double ended needle when its contents are to be expelled into the vial. The capsule and its cap are then removed and discarded. In an alternative arrangement, the cap of the capsule is coupled to the adaptor cap and the diluent introduced into the vial through a closure secured by the cap of the vial, after which the capsule is removed from the plunger and the latter is coupled to the piston. In further embodiments, the capsule is replaced by a shell vial. The open bottom of the vial is formed with a strengthening bead designed not to interfere with handling of the vials by conventional vial sterilizing, filling and capping machinery.

2 Claims, 14 Drawing Sheets



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4,116,240	9/1978	Guiney .	
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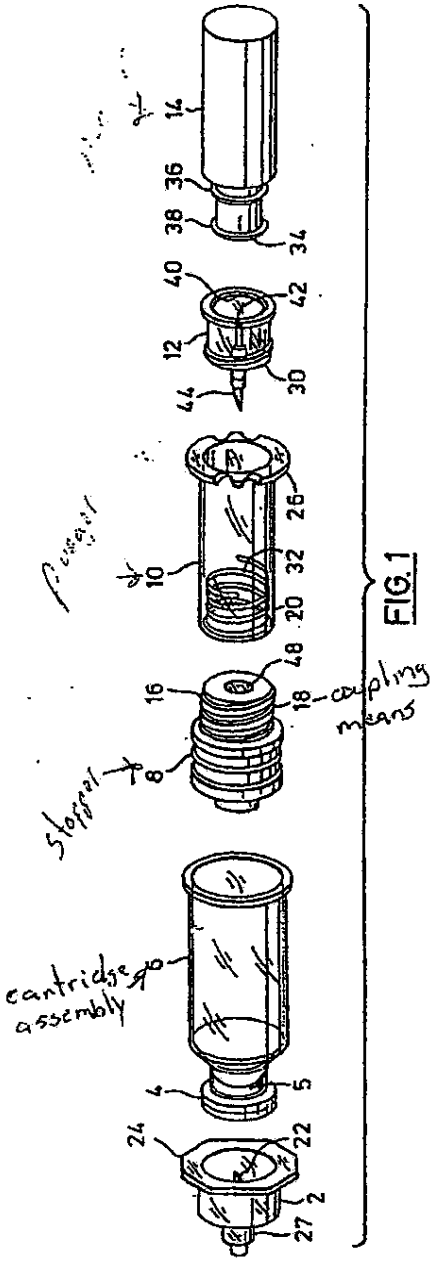
4,583,971	4/1986	Bocquet et al.	604/414
4,675,020	6/1987	McPhee	604/414
4,723,956	2/1988	Schnell et al.	604/408
4,731,068	3/1988	Fleese .	
4,755,169	7/1988	Sarnoff et al. .	
4,861,335	8/1989	Reynolds	604/191
4,886,495	12/1989	Reynolds .	
4,931,043	6/1990	Ray et al.	604/228
5,137,511	8/1992	Reynolds	604/88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coupling means
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stopper
cartridge assembly
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FIG. 1

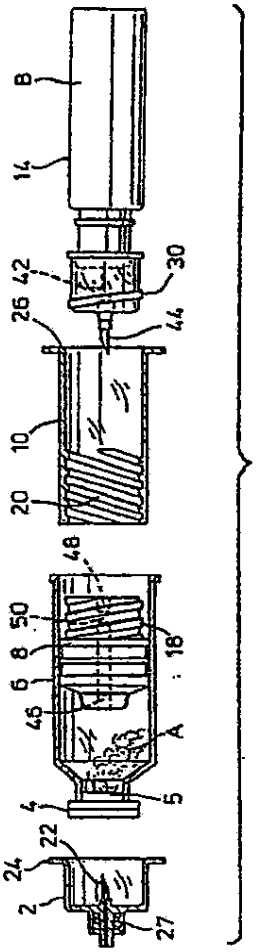
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FIG. 2

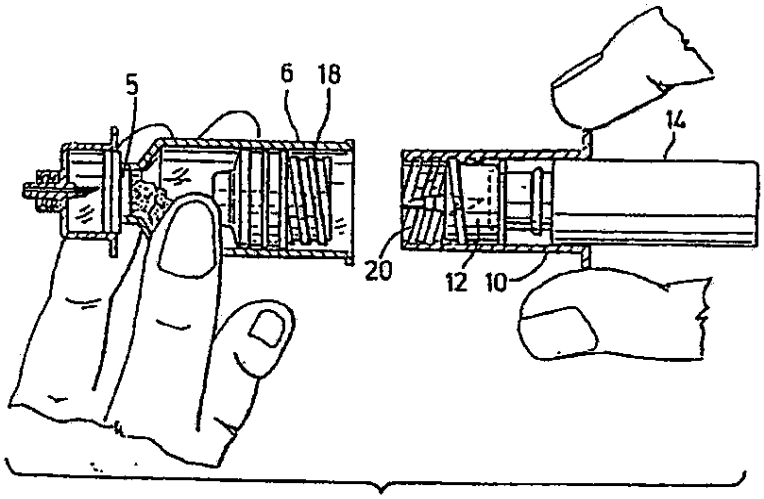


FIG. 3

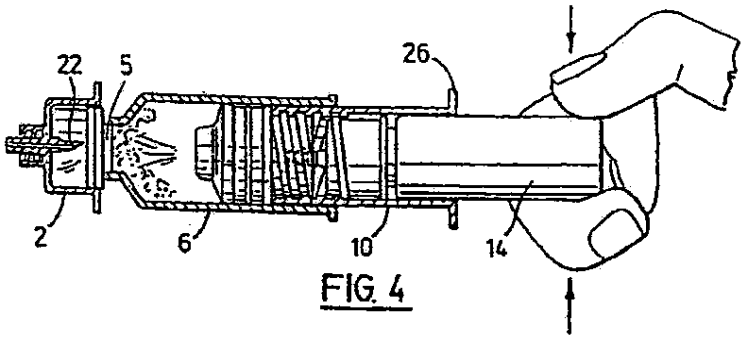


FIG. 4

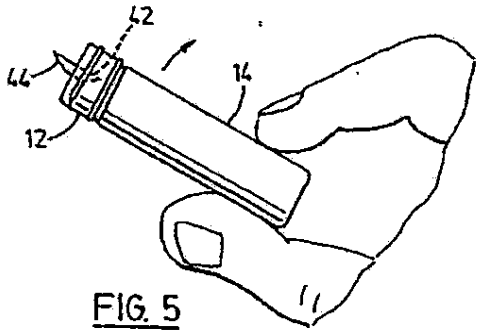


FIG. 5

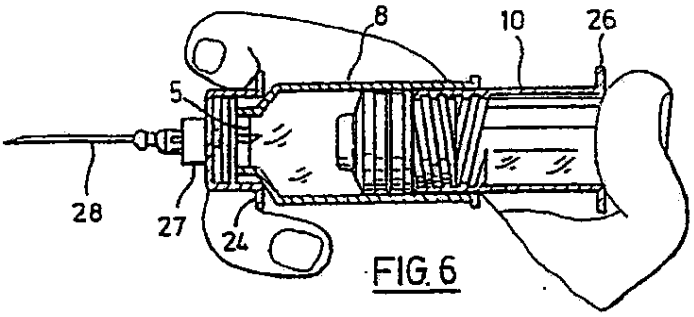


FIG. 6

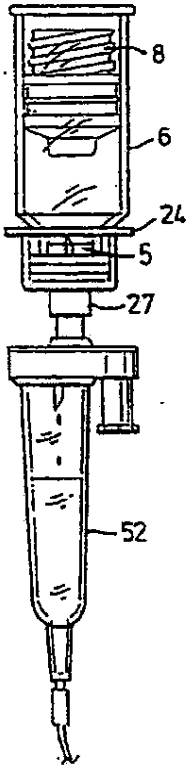


FIG. 7

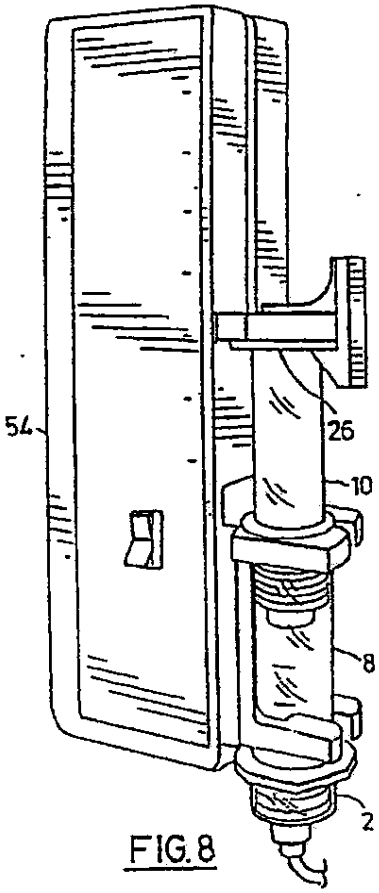
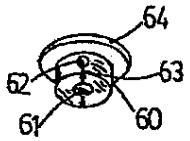


FIG. 8

FIG. 9



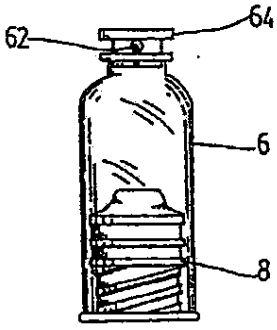


FIG. 10

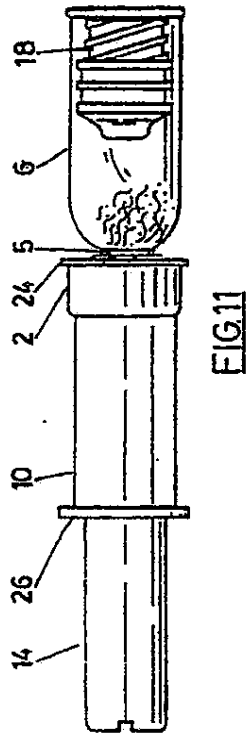


FIG.11

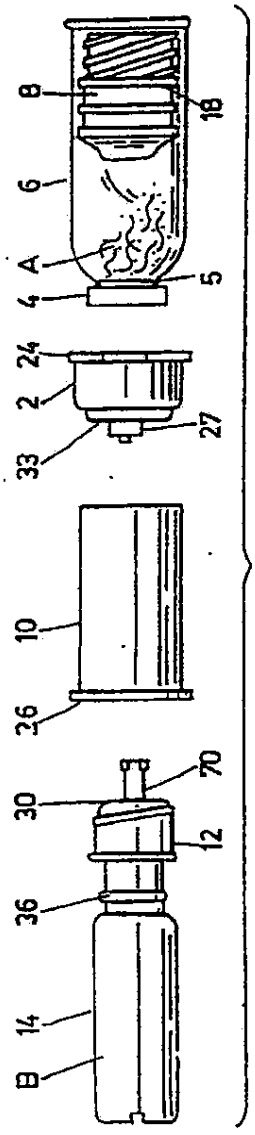


FIG.12

FIG. 13

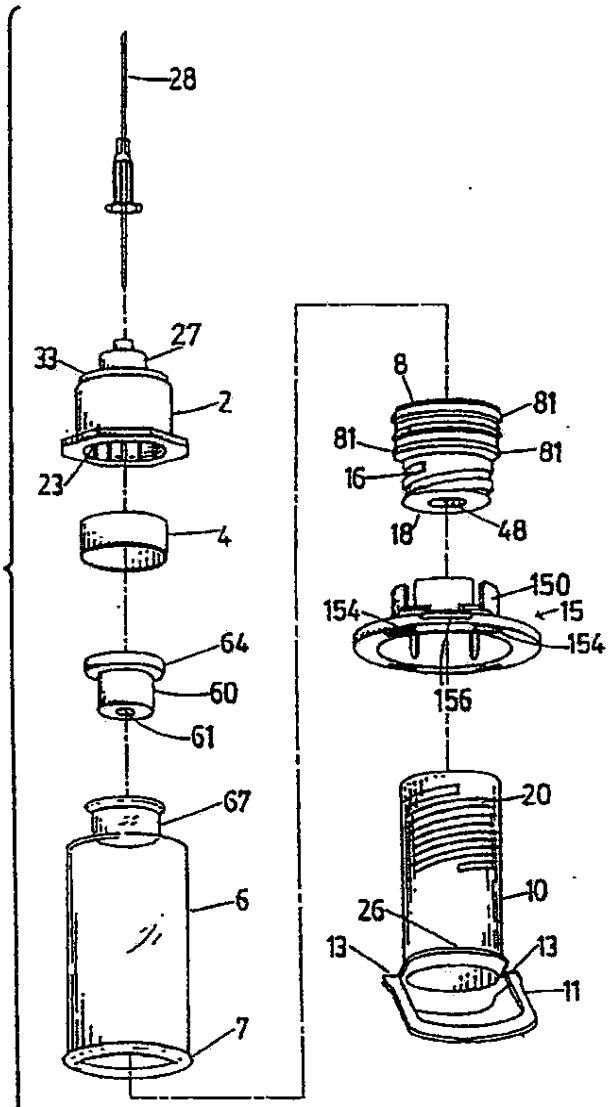

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FIG. 13

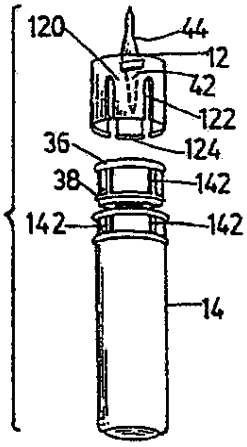
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FIG. 14

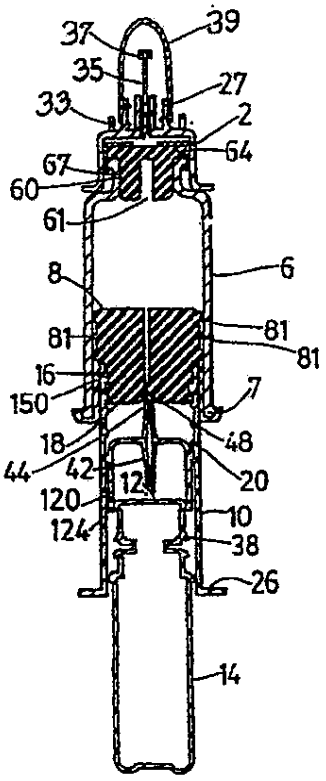
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FIG. 15

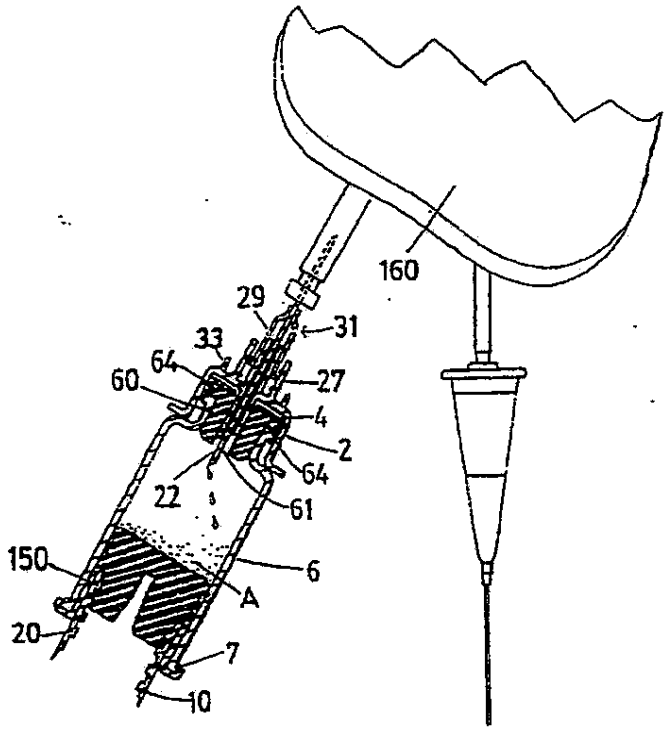

FIG.16

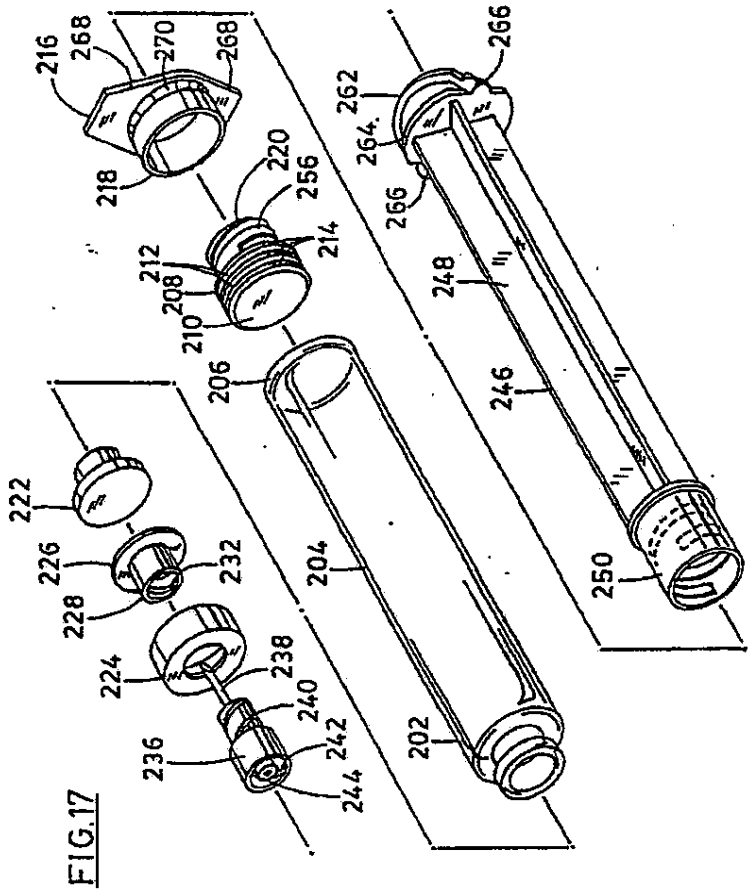
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FIG.17

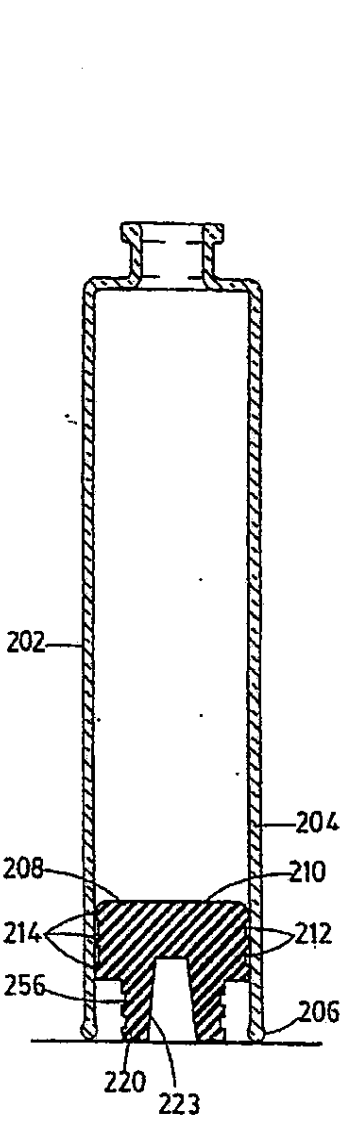
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FIG.18

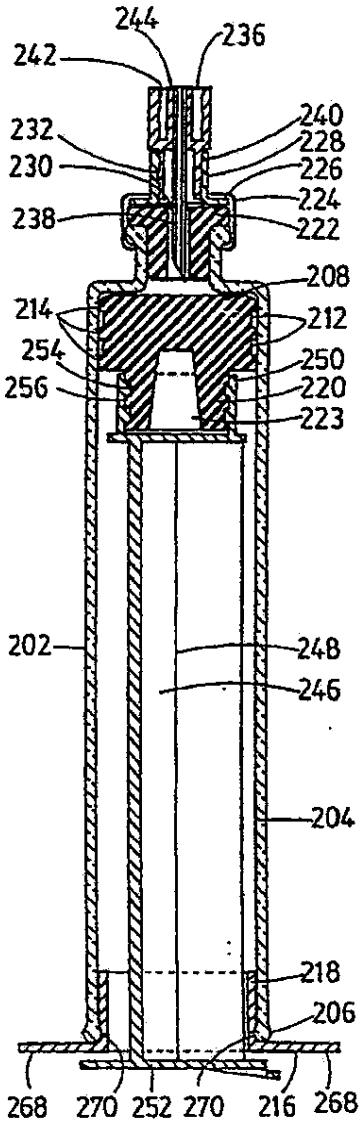
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FIG.19

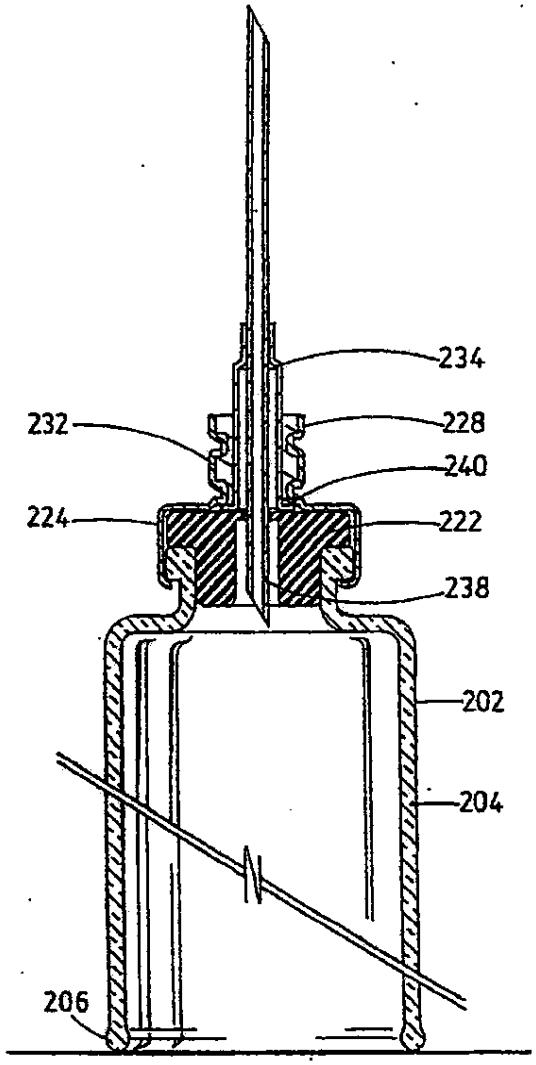

FIG.20

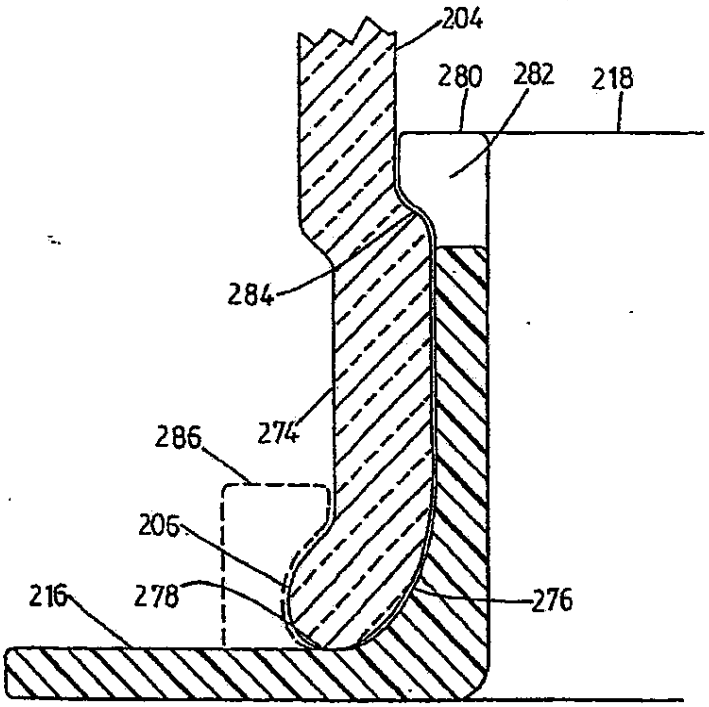

FIG.21

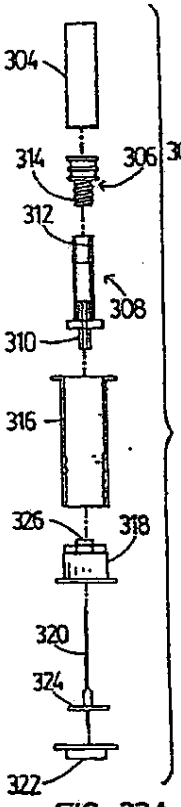

FIG. 22A

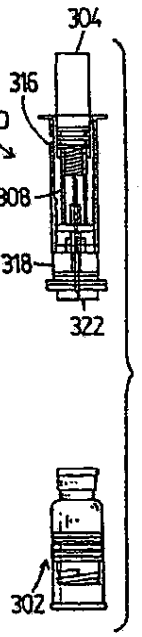

FIG. 22B

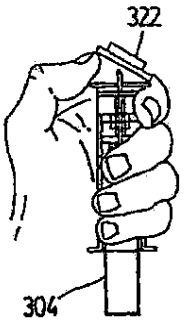

FIG. 22C

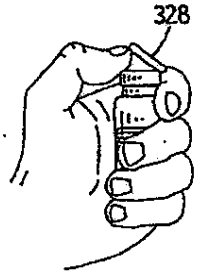

FIG. 22D

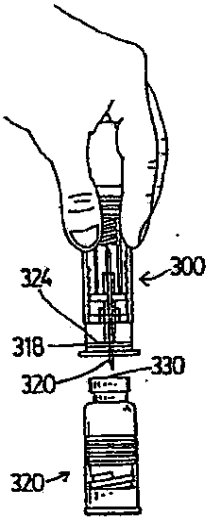

FIG. 22E

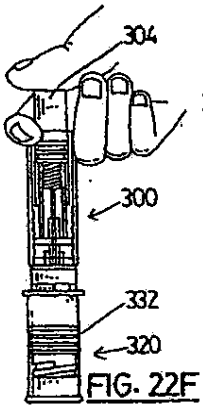

FIG. 22F

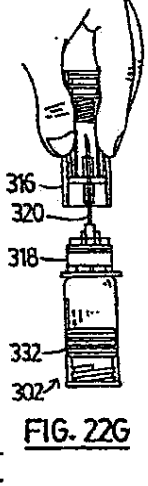

FIG. 22G

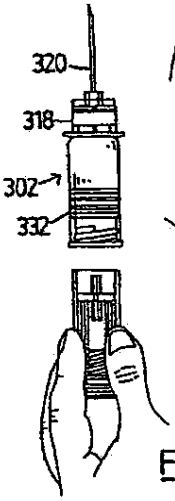

FIG. 22H

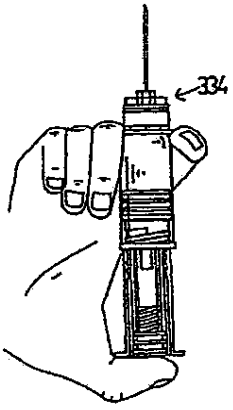

FIG. 22I

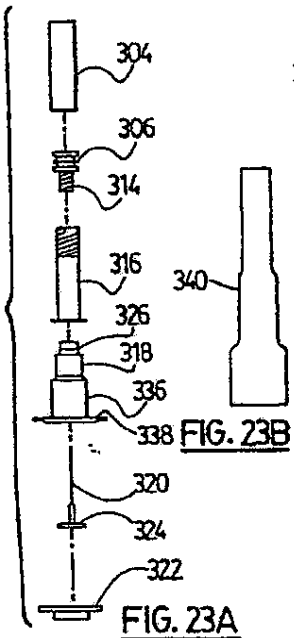

FIG. 23A

FIG. 23B

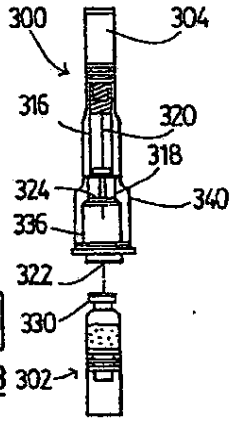

FIG. 23C

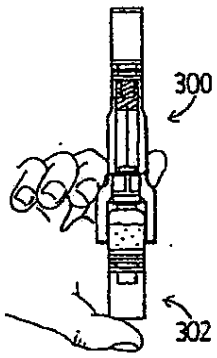

FIG. 23D

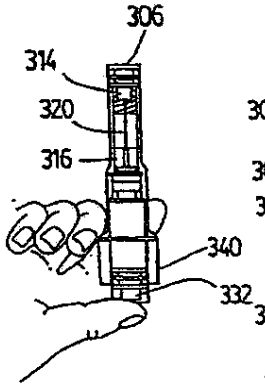

FIG. 23E

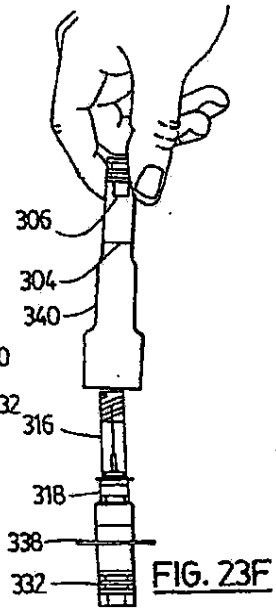

FIG. 23F

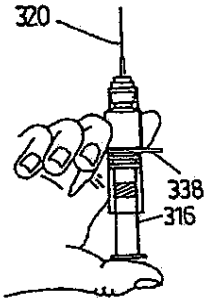

FIG. 23G

SYRINGE

REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of my co-pending application Ser. No. 07/437,203 filed Nov. 6, 1989, and now U.S. Pat. No. 5,137,511 which is a continuation-in-part of application Ser. No. 07/072,015 filed Jul. 8, 1987 and now U.S. Pat. No. 4,886,495.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to prefilled syringes for use in medical or veterinary treatment.

2. Review of the Art

There has been an increasing trend in recent years to the putting up of pharmaceuticals in dosage forms so as to minimize the preparation required to administer a medicament to a patient and to reduce the chances of dosage errors or contamination. One dosage form which has been gaining rapid acceptance is the prefilled disposable syringe. Various difficulties are however associated with the preparation and usage of such syringes, particularly in the case of preparations which, in ready to use condition, have a short shelf life. Numerous forms of dual compartment syringe structures have been proposed for the shipping of such preparations with components stored in separate compartments for admixture immediately prior to use. Although certain structures have met with some degree of acceptance, they are commonly difficult to manufacture and/or use because of difficulties in filling the syringe with the components, and because they require extensive manipulation immediately prior to use. Moreover they are frequently substantially more bulky than conventional syringes because in many cases they frequently comprise components which effectively represent two syringes in tandem.

Problems in the manufacture of prefilled syringes are not confined to two component systems and even with single component systems the filling of syringes under factory conditions is difficult to mechanize effectively and requires expensive special purpose syringe filling machinery. The same applies to related units prefilled with liquids required for injection or infusion during medical procedures.

Another approach where single component systems are involved is exemplified by British Patent Specifications Nos. 1,252,306 and 1,444,119, and U.S. Pat. No. 4,445,895, in which a prefilled cartridge having a displaceable plug at one end, and a needle penetrable closure at an opposite end, is inserted into the barrel of a syringe for dispensing of its contents. Whilst such cartridges and the equipment for filling them are known and available, they are only really suitable for preparations which can be stored in liquid form, and require either a special or a modified syringe for their use. The cartridges themselves require special filling apparatus.

In a further arrangement disclosed in U.S. Pat. No. 3,845,763, a cartridge or vial is closed at its bottom end by a slidable plug with a downwardly extending stem, which cartridge or vial is inserted bottom end first into a special holder which carries a double ended needle, so that the stem is penetrated by the needle and the body of the vial is converted into a plunger which can be depressed to expel the contents of the vial through the stem. The projecting stem means that the vial cannot be filled utilizing conventional vial filling machinery.

The high capital expenditure involved in implementing known prefilled syringe systems has severely limited their adoption to those few cases where their advantages outweigh the substantial additional unit costs involved as compared to conventional modes of delivery.

SUMMARY OF THE INVENTION

The present invention seeks to provide a system for the distribution of preparations required for injection or infusion in liquid dosage form during medical procedures, which has a wide range of utility both for single component liquid preparations or for two component systems of which one component may be a solid, which utilizes a small number of components all suitable for mass production using material already approved for usage in such applications, which is simple to assemble and can be filled utilizing equipment already available to most pharmaceutical manufacturers, which minimizes the number of "clean room" operations required, and which minimizes certification problems.

The system is based upon and built around a basic component in the form of a 'bottomless vial'. Such a bottomless vial has all of the characteristics of a conventional pharmaceutical vial, except that the glass base of the vial is replaced by a piston wholly received within the vial and designed to form a hermetic seal with its cylindrical side wall, the seal being maintained both when coupled and when uncoupled from a plunger releasably connectable to the piston for moving the latter axially of the vial. A particularly important characteristic of such a bottomless vial is that it can be conveyed, filled and capped reliably by conventional vial sterilization, filling and handling equipment such as is already possessed by most pharmaceutical manufacturers. To this end, the bottomless vial must be free of features which would significantly compromise its stability when handled by such equipment. A flange or bead is required around the base of the vial for various reasons, but must result in no more than a slight increase in the overall diameter of the vial, and must be configured so as to avoid any substantial increase in its tendency to tip when jostled by other similar vials, and the centre of gravity of the vial must not be displaced so far upwardly as to substantially reduce the stability of the vial.

I have found that it is important that the bottom end of such a bottomless vial terminates in a somewhat rounded peripheral bead, which serves several purposes. Firstly, it strengthens the open end of the vial and reduces stress concentrations and the risk of breakage, particularly during insertion of the piston. Secondly, the rounding produces a slight internal flare which facilitates piston insertion. Thirdly, it provides means for securely engaging a subsequently applied piston retainer which prevents possible ejection of the piston during shipping and storage of the vial due to gas generation or expansion within the hermetically sealed vial above the piston.

Whilst the provision of such a bead is thus highly desirable, conventional formation of the bead as an external projection on the body has the disadvantage increasing the diameter of the bottom of the body, thus both increasing the capability of tipping of the vials while being conveyed, and possibly providing a ramp for such tripping by riding over or under the beads of

adjacent vials unless the external configuration of the bead is carefully controlled. At the same time, particularly for syringes prefilled with a single component liquid pharmaceutical, there may be a requirement for a syringe capacity which requires the height to diameter ratio of the body to be increased as much as possible, which in turn requires maximum stability of the vial when conveyed free-standing.

The piston must be capable of maintaining a hermetic seal with the wall of the vial, of integrity comparable to that achieved during capping of a conventional vial, and this seal should be maintained in storage and during manipulation of a syringe system incorporating the vial, during which the piston may be subject to non-axial forces transmitted to it by a plunger and tending to break the seal.

In the context of the invention, it should be understood that "vial" refers to a particular type of container, having a rather squat cylindrical body whose height compared to the diameter of its base is such that it may stand stably on its base whilst being conveyed through a vial handling and filling machinery and whilst subsequently sealed and capped. Its body should also be free of external projections large enough to interact with other vials or the filling machinery in a manner such as to promote tipping. A vial has a neck with a large enough internal diameter to permit filling from a vial filling machine: solid filling materials will normally require a larger neck than liquids. Vials should not be confused with cartridges, which are comparatively long and slim, and cannot usually be filled utilizing vial filling machinery since they are too tall to rest in a stable manner on their bases. Cartridges also are typically thin-walled and lack a bead or flange, which renders them fragile, and makes it difficult to insert a piston without excessive risk of breakage.

Accordingly the present invention provides a vial formed of rigid transparent material and consisting of a cylindrical body, said body having an open bottom end having an external diameter at most only slightly greater than that of the remainder of the body, but sufficient relative to the height and centre of gravity of the vial as a whole to support the latter in a stable manner when conveyed standing on its open end through vial filling and capping machinery, injectable material within the body, a comparatively wide neck at the top of the body through which said injectable material is filled into the body, an external peripheral flange surrounding the neck, an elastomeric closure applied to the neck, a cylindrical cap clamped onto the flange of the neck and having an annular inward extending flange at a top end overlaying the closure to secure the closure to the neck with the closure presenting a needle penetrable central portion, an impervious substantially solid piston of resilient material sealingly received within said body at its lower end beneath said injectable material and above said open bottom end, and an extension integral with said piston, projecting downwardly from said piston but wholly within the body, for establishing a flexible connection to a syringe plunger in a zone between the piston and said open end of the body, whereby said vial may be converted into a syringe for ejection of the injectable material on movement of the piston towards the neck, by connection of said syringe plunger to said extension and connection of fluid conduit coupling means to said cylindrical cap.

According to a further feature of the invention, a vial for forming a barrel and a piston of a syringe comprises a cylindrical glass body having at one end an open neck and a peripheral external flange around an outer end of the neck, and a peripheral rounded bead at an open opposite end, and a piston having a cylindrical head within and concentric with the cylindrical glass body in slidable hermetically sealing relationship with the inner surface of the body, the piston being located to define a chamber of volume equal to the nominal capacity of the vial between the piston head and the neck of the vial, the piston having an integral axial flexible extension of lesser diameter than the head and extending towards but ending just short of said open opposite end of the body, the flexible extension being configured for releasable coupling with a socket at an end of a plunger, and the vial having at least sufficient stability, when standing on the peripheral bead, to pass reliably through conventional vial filling and capping machinery without tipping over, wherein the bead is formed so that the bead is at least partially inwardly of an interior surface of a side wall of the glass body, an external extent of the bead beyond the remainder of an external surface of the wall of the body being sufficiently slight to leave said external wall free of projections having an adverse effect on the stability of the vial.

The differences between such vials and a conventional vial do not prevent them from being filled and capped in conventional vial filling and capping machinery; indeed, apart from the replacement of the bottom wall of the vial by a piston as specified, it is a conventional vial, and can be handled normally by the machinery during filling with either liquid or solid material. The presence of the piston which is relatively massive, in the lower part of the vial even helps stabilize the latter during filling. Furthermore, liquid filled vials may be lyophilized utilizing special stoppers either as known in the art or as described below. Obviously the cubic capacity of such a vial is less than the capacity of a conventional vial of comparable overall dimensions but for most purposes this is immaterial.

The invention also extends to a method of packaging a pharmaceutical in a pharmaceutical vial formed of rigid transparent material with a cylindrical body and a comparatively wide neck at the top of the body, empty of pharmaceutical, in an upright position through conventional vial filling and capping machinery which fills the pharmaceutical into the body through the neck, applies an elastomeric closure to the neck, and applies a cap overlaying the closure to secure the closure to the neck to produce filled and capped vials, characterized in that to permit subsequent administration via injection direct from the vial, a cylindrical side wall of each uncapped empty vial is formed so as to define a bottom opening in place of an integral bottom wall of the vial, with a bead adjacent the bottom opening, any external projection of the bead relative to the outer wall of the vial being too small to cause substantial instability of the vial when conveyed upright adjacent other similar vials during filling and capping, a cylindrical substantially solid piston of resilient material is slidably lodged prior to filling of the vial wholly within the cylindrical side wall above said bottom opening so as to form a hermetic seal with the side wall, an internal and axial extension from the piston, of lesser diameter than the piston and adapted for subsequent coupling to a syringe plunger, is oriented so as to extend downwardly towards the bottom opening.

A vial in accordance with the invention may be converted into a syringe by the addition of a plunger cou-

pled to the piston and an outer cap which acts as a needle carrier. More specifically, the syringe includes as well as the vial a syringe plunger connected to the flexible extension from the piston, and an outer cap engaged over the cap of the vial, the outer cap having a hollow needle projecting axially within the cap and a coupling for engagement with injection means and communicating with said hollow needle, the outer cap being axially movable relative to said cap of the vial from a position in which the needle ends short of the cap of the vial to a position in which it penetrates the cap of the vial. The plunger is provided with radially extending flanges for sustaining actuating forces applied to the syringe through a flange grip provided on the outer cap or on a plunger guide or piston stabilizer ring applied to the open end of the vial.

In a syringe for a two component medicament, it is necessary to provide for packaging of the second component and its admixture with the first component in the vial prior to dispensing. The invention thus further extends to a capsule assembly comprising a generally cylindrical sealed capsule having walls formed of a flexible needle penetrable material of suitable properties, a generally cylindrical neck defined by said walls at one end of the capsule, said neck having axially spaced inner and outer peripheral ridges, and a generally cylindrical cap applied to said neck so that a detent within the cap engages the outer peripheral ridge on the neck, a hollow cannula being formed integral with and passing through said cap so that an inner penetrating end within the cap ends short of the neck of the capsule and an outer end formed either in the form of a needle or a fluid coupling which extends outwardly of the cap, the cap being displaceable relative to the capsule to a position in which the detent rides over the inner ridge and the inner end of the needle penetrates the neck of the capsule, the cap and capsule being of a diameter such that they can enter the tubular plunger to a position in which the outer end of the cannula, if of needle form penetrates the septum of the piston when the plunger is engaged with the latter. An alternative arrangement may be used where the outer end of the cannula is a coupling, in which case the latter is connected to the coupling on the outer cap of the syringe, with the plunger being used as a support for the capsule prior to being coupled to the piston.

Thus the injection system comprises a sequence of components of which various sub-sequences can be combined to form injection systems for preparations requiring shipping and storage as two separate components, certain sub-sequences themselves having utility respectively as injection systems for single component liquid preparations. "Injection" is utilized broadly to cover hypodermic, intramuscular and intravenous injection, gravity and mechanical infusion, and injection into other vessels utilized in medical treatment or testing. For the purposes of description, the "front" or "top" end of an injection system will be considered the end of the system from which a liquid preparation is so injected.

The arrangement including the capsule assembly has a number of advantages in the manufacture and use of prefilled syringes for two component systems; furthermore, without the third cap and the sealed capsule containing the second component the remaining components provide, according to a further feature of the invention, advantages in the manufacture and use of prefilled syringes for single component systems. The third cap and sealed capsule provide, according to yet a further feature of the invention, an advantageous subsystem for various applications in which a sealed sterile source of a liquid is required for injection, or dropwise introduction into other containers used in medical procedures. With prefilled syringes for two components systems, either the capsule or the capsule and the third cap, may be sold, or shipped separately. This enables different diluents or sizes of capsule to be selected, or a common set of diluent capsules to be utilized with syringe assemblies containing different first components, thus simplifying inventory control.

As an alternative to the use of capsules, shell vials may be utilized in an advantageous manner.

Further features of the invention will become apparent from the following description of a preferred embodiment thereof with reference to the accompanying drawings.

SHORT DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective exploded view of the mechanical components of a syringe system including a vial in accordance with the invention;

FIG. 2 is a partially longitudinally sectioned, partially exploded view of the syringe components showing some further details of their construction;

FIGS. 3, 4 and 5 illustrate preparation of the syringe system to provide a syringe ready for use;

FIGS. 6, 7 and 8 illustrate exemplary applications of the syringe;

FIGS. 9 and 10 illustrate an optional feature of a vial in accordance with the invention;

FIGS. 11 and 12 are elevational and exploded views of an alternative embodiment of the syringe system;

FIG. 13 shows the separated parts a further embodiment of the syringe system;

FIG. 14 shows, separated, a diluent capsule and cap for use with the system of FIG. 13;

FIG. 15 is a longitudinal cross section through the assembled system of FIGS. 13 and 14;

FIG. 16 is a fragmentary view of a syringe in accordance with the invention utilized in conjunction with an I.V. bag;

FIG. 17 is an exploded isometric view of the components of a first embodiment of the syringe;

FIG. 18 is a vertical section through a vial portion of the syringe, ready for filling;

FIG. 19 is a longitudinal section through an assembled syringe, after discharge of its contents;

FIG. 20 is a fragmentary longitudinal section on an enlarged scale of a portion of the syringe shown in FIG. 3, showing a modification of the arrangement shown in that Figure; and

FIG. 21 is an enlarged vertical section through the head of a second embodiment of the syringe, also showing adjacent parts of a modified piston retainer and finger grip.

FIGS. 22A through I illustrate one mode of utilizing a shell vial in conjunction with a vial in accordance with the invention to provide a syringe system; and

FIGS. 23A through G illustrate a second mode of utilizing a shell vial in conjunction with a vial in accordance with the invention to provide a syringe system.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring to FIGS. 1 and 2, a syringe system for the injection of a liquid preparation stored as two compo-

nents comprises seven primary mechanical components, apart from the components of the preparation, which latter are shown in FIG. 2 but not FIG. 1. The components of the preparation typically comprise a first component A which may be in any physical state suitable for storage in vial, and a second liquid component B, typically but not necessarily sterile water. The liquid component B is stored in a sealed capsule 14 of flexible material, manufactured using conventional techniques from a material, usually synthetic plastic, which is compatible with the contents of the capsule. The first component is stored in a cylindrical vial 6, typically of glass, and capped by an annular cap 4 which retains a conventional needle penetrable sealing member accessible through a central opening in the cap. By a vial is meant a cylindrical vessel which can assume a stable upright position supported by its base, the overall height of the vessel exceeding the external diameter of the rim of its base by a factor sufficiently small that it remains stable when passing through conventional vial filling and capping equipment utilized to fill and cap the vial. This factor preferably does not exceed 2.5 for the present embodiment, but can be increased by means discussed further with reference to FIGS. 17-21. A neck at the upper end of the vial 6, which is capped by the cap 4, has a relatively internal diameter characteristic of such vessels, usually not less than about 7.5 mm for liquid or 10 mm for solids, so that filling with either liquids or solids can be readily achieved. The cap 4 is formed by an aluminum sleeve, having a flange retaining a sealing member formed by a soft rubber disc or plug 5 over or in the front end opening, and tightly crimped onto a neck at the front end of the vial so as to seal the latter. A major difference from conventional vials is that the conventional bottom wall of the vial is replaced by an axially movable piston 8 wholly within the vial and in sealing contact with the vial walls. When received within the vial 6, this piston in no way interferes with the handling of the vial using conventional machinery, and in particular permits the vial to be stood on its base with its neck (which forms the front end of the vial when in use) upwards as it passes through the filling and capping equipment.

The filled vial 6 may be converted into a prefilled syringe by applying an outer cap 2 over the cap 4 and positively attaching a cylindrical plunger sleeve 10 to the piston 8. The piston 8, typically formed of rubber, is moulded with a rearward extension 16 with an external thread 18, whilst the interior of the front end of the plunger sleeve 10 is formed with a complementary internal thread 20 so that it may be screwed onto the piston 8. The outer cap 2 fits over the inner cap 4 so that a hollow needle 22 formed within the cap 2 does not reach the penetrable zone of the cap 4. On the front of the cap 2 and in communication with the hollow needle 2 is a coupling adapter 27, for example similar to those sold under the trade mark LUER-LOK, for connection of the syringe to a needle 28 or other instrumentality (see FIGS. 6-8). To prepare the syringe for use, the outer cap 2 is pulled back over the inner cap 4 so that the needle 22 penetrates the cap, and the needle 28 or other instrumentality is applied. This should be done without pressing on the plunger sleeve so as to avoid accidental ejection of the contents of the syringe. The rear ends of both cap 2 and the sleeve 10 are formed with radially extending flanges 24 and 26 respectively which form finger grips for operation of the syringe. Thus if a user grips the syringe by the flanges as shown in FIG. 6 and presses them towards each other, the contents of the syringe can be expelled through the needle 22 and the needle 28. It will be noted that the rear end of the vial 6 is formed with only a relatively slight external bead 7 rather than the wide finger flange commonly found on the barrels of conventional syringes. In the present arrangement, the flange 24 provides the function of such a finger flange, enabling the bead 7 to be reduced to a size which will avoid such interference between the flanges of adjacent vials as would cause tipping when the vials are conveyed in a vertical attitude through filling and capping equipment.

In many applications, it is desirable to prevent premature penetration of the plug 5 by the needle 22, and therefore the cap 2 may be moulded with short internal threads (not shown) which prevent rearward movement of the cap 2 unless it is twisted so that the threads bite into the soft aluminum of the cap 4 and draw the cap 2 rearwardly so that the needle 22 can penetrate the plug.

A prefilled syringe constructed as discussed above has significant advantages over conventional prefilled syringes in that the vial may be filled using conventional vial filling equipment, and yet may be utilized directly instead of requiring its contents to be transferred to a syringe prior to use as has been conventional in the use of vials.

The vial may also be charged with material which is not directly injectable, such as solids which must be dissolved or suspended in a liquid medium prior to injection. In this case the liquid medium is sealed as already described in a flexible capsule 14. A third cap 12 is either applied to the capsule as shown in FIG. 2, or inserted into the plunger sleeve 10 so that a screw thread 30 on the exterior of the cap engages the screw thread 20 within the sleeve.

A neck 34 of the capsule 14 has two peripheral ridges 36 and 38. If the cap 12 is applied to the capsule, a detent 40 within the cap is pushed over only the outer ridge 38 so that a rear end portion 42 of a hollow needle mounted in the cap stops short of the end of the capsule. By forcing the detent 40 rearwardly over the ridge 36, the needle portion 42 can be forced rearwardly so as to penetrate the capsule. A forward end portion 44 of the hollow needle has a length such that when the cap 12 is screwed into the sleeve 10, and the sleeve 10 is screwed onto the piston 8, the needle portion 44 penetrates a resilient septum 50 normally separating axial passages 46 and 48 formed in the front and rear of the piston.

In use, if the capsule 14 and cap 12 are shipped as a separate unit, this unit is screwed into the sleeve 10 (see FIG. 3), and the sleeve 10 is pushed into the rear of the vial 6 so that the needle portion 44 penetrates the septum 50 of the piston 8 and the thread 20 is screwed onto the thread 18 of the piston (see FIG. 4). This action also substantially unscrews the cap 12 from the thread 20. The capsule 14 is then pressed forward onto the needle portion 42, and the liquid contents of the capsule can then be squeezed through the needle and into admixture with the first component in front of the piston 8. Thereafter the capsule 14 and cap 12 may be pulled as a unit from the sleeve 10 and discarded (see FIG. 5). The septum 50 reseals as the needle portion 44 is withdrawn, leaving a syringe ready for use as illustrated in FIGS. 6-8. Alternatively, if the cap 12 is prefitted to the sleeve, the sleeve 10 may be screwed onto the piston 8, and the capsule 14 pressed into the sleeve 10 and the cap 12 so as to establish communication between the capsule

claim 1

claim 1

and the space forward of the piston, the procedure thereafter being the same.

Rather than being used conventionally with a needle as shown in FIG. 6, the prepared syringe may be used for gravitational or mechanical infusion as shown in FIGS. 7 and 8. In FIG. 7, the adapter 27 is fitted to a complementary coupling on a gravity infuser 52 to provide a drip feed, the sleeve 16 having been unscrewed and discarded, together with the cap 12 and capsule 14, if used. In FIG. 8, the syringe is mounted in a mechanical infuser 54 such as that sold under the trade mark BARD, the latter being equipped with clamps 56, 58, 60 suited for engagement with the syringe.

By basing the system on an open-bottomed vial 6 closed at its bottom end by a piston 8 equipped with means such as the screw thread 18 for coupling it to a plunger of sleeve form, and with a needle penetrable septum 50, in optional conjunction with sealed flexible capsules of diluent, great flexibility in application can be obtained, using components which are easy to fill, compact to ship, and easy to make ready for use.

Referring now to FIGS. 9 and 10, the rubber disk or plug retained by the cap 4 on the vial 6 may be replaced by a modified plug 60 as shown in perspective from beneath and one side in FIG. 8, and partially installed on a vial 6 in FIG. 9. Use of such a plug 60 is advantageous when the solid component of a medicament is to be prepared in situ in the vial by lyophilization. The vial is filled with a liquid preparation to be lyophilized, and plug 60 inserted to the position shown in FIG. 9, so that the interior of the vial communicates with its environment through a central passageway 61 and radial bores 62, the passageway and the bores being no larger than needed for the removal of water vapour during lyophilization. The plug is split at 63 to facilitate moulding. After filling the contents of the vial are rapidly frozen and vacuum dried to leave a solid residue in the vial which can be reconstituted immediately before use. The plug 60 is then moved to the full extent permitted by a flange 64 into the neck of the vial 6 and secured by a cap 4. Whilst a conventional lyophilization stopper could be utilized in place of the plug 60, the latter has the advantage of minimizing the amount of liquid trapped within the stopper during use of the syringe. For the same reason, the head of the piston 8 is shaped so as to minimize dead space in the neck of the vial when the contents of the vial are expelled during use of the syringe.

FIGS. 11 and 12 illustrate an alternate configuration of the syringe. The various components are essentially identical to those already described, and the same reference numerals are utilized except that the outer needle 44 of the conduit extending through the cap 12 is replaced by an extension 70 which is configured at its outer end to couple with a standard syringe coupling such as the coupling 27 on the cap 2. This enables the capsule 14, once inserted in the plunger 10, to be locked through the extension 70 and the coupling 27 to the cap 2 to produce the compact assembly shown in FIG. 11. The inner end of the plunger 10 is a press fit on an annular retaining flange 33 formed on the cap 2. To prepare the syringe for use, the cap 2 is forced rearwardly over the cap 4 so that the needle 22 (see FIG. 2) pierces the seal 5, and the capsule 14 is forced forward so that it is pierced by the needle 42 and its contents can be expelled through the needle 42, the extension 70, the coupling 27 and the needle 22 into the vial 6. The assembly of the capsule 14 and the plunger 10 can then be released from the remainder of the syringe by turning so as to release the extension 70 from the coupling 27, a needle (not shown) may be applied to the coupling 27, the capsule 14 is removed from the plunger 11 and discarded, and the plunger 11 is screwed onto the coupling 18 to ready the syringe for use. With this arrangement, the passage 46 in the piston 8 is not required, although the passage 48 may be retained to save material and enhance the flexibility of the extension 18 of the piston.

A similar arrangement may be utilized for single component medicaments in which case the capsule 14 and cap 12 are not provided. The arrangement is advantageous for both single and multiple component medicaments since only the vial need be assembled and filled in a clean room, the only additional step required over the filling of a conventional vial being the insertion of the piston 8. The plunger 10 may be pressed onto the cap 2, and this assembly, if desired together with a needle and/or a capsule 12 and cap 14, may be separately sterilized and packaged, without endangering the stability or destroying the contents of the vial, which will often be sensitive to heat or radiation utilized for sterilization purposes. Since the capsule 12 can withstand conventional terminal sterilization techniques (see further below), it can be sterilized independently of the vial. This is a major advantage over many two-component syringe systems in which the components are separated only by some form of penetrable plug or diaphragm and must therefore either be fully assembled in a clean room, or subjected in assembled form to terminal sterilization techniques which may destroy or damage a component of the pharmaceutical preparation.

Where the capsule 12 is not being used, it is possible to utilize a cap 2 in which the needle 22 is not provided, and instead use a needle arrangement as shown in FIG. 13 or FIG. 15.

Features of presently most preferred embodiments of the invention are shown in FIGS. 13–15. The same reference numerals are used to denote the same parts in these figures as in the previous embodiments, where applicable, and construction and operation are similar except where otherwise indicated.

FIGS. 13–15 show a further vial and syringe system according to the invention, the vial comprising a body 6 of rigid transparent material, usually glass although synthetic plastic resins might be utilized in certain applications. The body has the general configuration of a conventional vial except for the absence of a bottom wall. In order to compensate for the strengthening effect which would be provided by the bottom wall, in order to provide a detent for an optional plunger stabilizer ring 15 described further below, and in order to permit a slight flare at the extreme bottom end of the vial, a rounded bead 7 is provided around the perimeter of the bottom end of the body, although its peripheral extent should not be sufficient to increase substantially the diameter of the vial or decrease substantially its stability during handling.

A medicament A is retained within the vial by a piston 8. A closure 60 substantially fills a neck portion 67 of the vial after the vial, closed at the bottom by the piston, has been filled through its neck portion by a conventional vial filling machine. Although the medicament shown is a solid, it may be a liquid, or filled as a liquid and lyophilized to leave a solid residue. The piston 8 is moulded from rubber, preferably of at least 50 durometer hardness, and is formed with multiple, preferable three, peripheral ribs 81 on its outer surface, the

external diameter of the ribs being slightly greater than the internal diameter of the body 6 so that an hermetic seal is established when the piston is pressed into the bottom of the body, initial entry being assisted by the flare mentioned above. The piston is moulded as a substantially solid body so that it has sufficient rigidity to maintain the desired hermetic seal with the body, any central bores within the piston (see FIG. 15) required to assist needle penetration being of insufficient radial extent to have any significant effect on its rigidity. Although in the piston shown in FIG. 16, a central bore 48 does just extend into the piston proper, its axial extent within the piston and its diameter are sufficiently small relative to the piston diameter that the rigidity of the piston is not substantially reduced. The longer bore 46 through the piston shown in FIG. 15 is of even smaller diameter so as not to prejudice piston rigidity.

The piston has a downward extension 18 of reduced diameter, in which the bore 48 is also present. The diameter of the bore 48 forms in this case a greater portion of the diameter of the extension 18, whose flexibility is thus somewhat increased by its presence. The extension carries on its outer surface a multistart thread, defined by grooves 16 which terminate abruptly short of the piston, forming abutments serving a purpose discussed further below. Provided that the hardness and rigidity requirements for the piston as a whole are met, the rubber utilized to form the piston, and any external coating on the rubber (which may act to increase the effective hardness of the rubber), are selected for compatibility with the medicament contained in the syringe, a number of approved materials being available and well known in the pharmaceutical art.

The neck closure 60 may be formed of similar rubber, and is similar in construction to that shown in FIGS. 9 and 10 if lyophilization of the syringe contents is required: otherwise the slot 63 and bores 62 (see FIG. 9) may be omitted. After insertion of the closure 60, its flange 64 may be held in place by a conventional cap 4 crimped over the flange and a flange on the neck of the bottle. Such a cap 4 may have a flip-off top attached to a separable central portion of the cap, partially severed from the remainder of the cap so that these portions may be broken away prior to assembly of the syringe to expose a central needle penetrable zone of the closure 60 above the bore 62.

The piston together with its extension 18 is relatively massive, with a weight which typically amounts to at least a major portion of that of the body 6. This weight in the lower part of the body assists in stabilizing the vial during handling and filling and further inhibits tipping.

As mentioned above, vial assembly and filling will normally be performed in a clean room, since many pharmaceuticals will not withstand terminal sterilization procedures. The only additional step which requires to be carried out in the clean room other than is conventional in the filling of vials is the insertion of the piston 8.

In order to convert the basic vial into a syringe system, either one of two different approaches can be used, similar respectively to those described with reference to FIGS. 1 to 6 and FIGS. 11 and 12 above. Only the differences from that corresponding to FIGS. 1 to 6 will be described in detail for the present embodiment, since the differences from the system of FIGS. 11 and 12 arrangement will in general be similar. FIGS. 13 and 14 show the components of a syringe system separated, whilst FIG. 15 shown them assembled and sectioned (although an alternative needle arrangement is shown in FIG. 15). It should be understood that the diluent cartridge 14 and cartridge cap 12 are optional features of the system and will only be utilized when a diluent or solvent is required for the content of the vial which is not provided by some other means. When building a system similar to that shown in FIGS. 11 and 12, the same parts will be used, except that if the cartridge 14 and the cap 12 are used, the cap 12 will be modified in the manner illustrated in FIGS. 11 and 12. Assembly in the manner described with reference to FIGS. 11 and 12 has the advantages already described.

Referring to FIGS. 13 and 15, an outer cap 2 is pushed over the cap 4, and is similar to that shown in FIGS. 1, 2 and 12, except that the internal needle 22 shown in FIGS. 1 and 2 is omitted, the syringe being utilized with an alternative needle arrangement. In FIG. 13, a conventional double ended needle 28, is shown, the inner end of which replaces the needle 22.

FIG. 15 shows an arrangement in which the needle 28 may be single ended, an auxiliary hollow needle 35 being provided with a cylindrical sleeve 37 at the top which replaces the outer extremity of the inner portion of the coupling 27. A cap 39 is provided to retain the needle 35 within the coupling 27 until the needle 28 is fitted. When the syringe is to be used, the cap 39 is removed, and the sleeve of the needle is placed over the sleeve 37 and pushed down so that the needle 35 can penetrate the top of the vial and the needle 28 can be engaged with the coupling 27.

These needle arrangements are preferred for a syringe which is shipped in an essentially ready-to-use form, since the cap 2 may be pushed fully onto the cap 4 during assembly, yet the closure 60 remains unpenetrated until the needle (or other instrumentality as discussed below) is fitted at the time of use. On the other hand, the integral needle 22 is convenient where the assembly is to be utilized in the manner shown in FIGS. 11 and 12 and a capsule 12 is utilized. The inner surface of the cap 2 is provided with longitudinal ribs 23 which indent the soft aluminum of which the cap 4 is typically fabricated, and help retain the cap 2. The portions 41 and 43 of the cap 4, if present, are of course broken away prior to application of the cap 2.

The cap 4, closure 60, vial body 6 and piston 8 have already been described in detail above. The plunger 10 differs from that shown in FIGS. 1 and 2 in two respects. Its internal threads 20 end abruptly at abutments short of the front end of the plunger, so that when the plunger is screwed onto the extension of the piston, the abutments at the ends of the threads meet abutments at the ends of the external grooves on the extension which grooves in this embodiment stop short of the inner end of the extension, just before the inner end of the plunger contacts the rear surface of the piston. This prevents the plunger being screwed excessively tightly against the back of the piston in a manner which might result in rocking movements of the plunger being transmitted directly to the piston. Instead such movements are largely absorbed by the flexibility of the extension 18. Secondly, the flange 26 at the rear end of the plunger is moulded so that about one half of its periphery is separated into an integral loop 11, which can be flexed rearwardly about hinge lines 13, and serves either as a thumb loop to assist manipulation of the syringe, or a suspension loop from which the syringe can be hung during infusion of its contents as discussed further below. The synthetic plastic material from which the

plunger is moulded is selected from those having hinge forming capability such as many pharmaceutically acceptable grades of polypropylene.

In order to provide further stabilization of the plunger, to prevent its withdrawal from the body, and to provide a finger grip during manipulation of the syringe, particularly where longer vial bodies 6 are utilized, an optional plunger stabilizer and adapter ring 15 may be provided. This has axially extending inner flanges 150 which enter the inner end of the body, and retaining lugs 152, which snap over the bead 7. Openings 154 and flanges 156 may be provided on the rear surface of the ring, as required, to assist in adapting the syringe to infuser apparatus such as that shown in FIG. 8.

Where the contents of the vial are liquid and do not require reconstitution or dilution, or reconstitution is effected by a diluent or solvent introduced via a needle or cannula through the closure 60, the cartridge cap 12 and diluent cartridge 14 are not required, the components already described constituting a complete syringe system. Otherwise these components may be provided and utilized as already described in relation to the embodiments of FIGS. 1 to 6 or FIGS. 11 and 12. The components themselves are however somewhat modified as shown in FIG. 14, to facilitate handling. A skirt portion 120 of the cap is formed with longitudinal slots 122 extending from its rear edge, and inner lips 124 around the inner periphery of that edge, whilst a front extension of the cartridge 14 is provided with ribs 142 extending longitudinally between the peripheral ridges 36 and 38, which ribs are accommodated by the slots 122. The ribs 142 are continued beyond a peripheral groove behind the ridge 36. The threads 30 and the cap 12 are reduced to short ridges between certain of the slots 122. Because of the slots, the cap 12 is readily engaged over the ridge 38, but when the assembly is inserted into the interior of the plunger 10, the diameter of the cap relative to the internal chamber of the plunger 13 such that the lip 124 is pressed into the ring of shallow recesses defined between the ridges 36 and 38 and the ribs 142, thus ensuring that the threads 30 may be engaged with the threads 20 within the plunger by turning the capsule, and inhibiting accidental forward movement of the cartridge 14 into the cap 12. Further turning of the capsule drives the needle 44 forward into the bore 48 (see FIG. 14) and thence through a septum in the bore into a small diameter counterbore 46 through the head of the piston (similar to that shown in FIG. 2), a piston modified in this manner being utilized when a diluent cartridge is to be used. The cartridge can then be forced forward so that the lips 124 ride over the ridge 38, permitting the needle 42 to penetrate the capsule whose contents can then be transferred to the vial by squeezing and/or aspiration.

Provided that the cap 12 is provided with a coupling 70, the capsule can of course also be utilized as described with reference to FIGS. 11 and 12, in which case the passage 46 in the piston is not required.

The capsule 14 is blow moulded from a heat sealable, film grade, low melting, high ethylene random propylene-ethylene copolymer suitable for medical use. An example of such a material, already approved for pharmaceutical applications, is DYPRO (trade mark) polypropylene Z9350 from Fina Oil and Chemical Company which has a melting point of about 130° C. Such a material, formed by injection of ethylene into a propylene matrix, combines necessary qualities of transparency, impermeability and flexibility with the stability to withstand sterilizing temperatures in an autoclave, despite its low melting point; the pressure in the autoclave is maintained at a sufficient level to prevent bursting of the capsule during sterilization. Conventional capsule materials are unsuitable for use in this application, since they lack at least one of the necessary properties of flexibility, transparency, impermeability, penetrability, compatibility with conventional pharmaceutical diluents, and ability to withstand sterilization temperatures without failure or degradation.

Utilization of syringes incorporating the above described modifications is similar to that of the other embodiments already described. The contents of the syringe may be delivered as already described with reference to FIGS. 6, 7 or 8, or in other ways. With a small modification to certain of the syringe components, the syringe contents may be reconstituted or diluted with fluid from an I.V. bag or minibag 160 and then injected into the bag for delivery, as shown in FIG. 16. Both the inner and outer components of coupling adaptor 27 of the cap 2 are elongated, and the bores of the inner component of the coupling adaptor and of the needle 22 are sufficient to provide an air venting passage around the read end of the needle 22 when fitted to the adaptor 27. A locking sleeve 29 on the needle 22, which sleeve engages the adaptor 27, is provided with a ventilation opening 31, such that when the sleeve 29 is screwed partially onto the adaptor as shown, air can escape through the sleeve as fluid from the bag 160 enters the syringe through the needle 22. When a desired amount of fluid has entered the syringe, the ventilation opening is closed by screwing the needle further onto the adaptor, following which the contents of the syringe may be injected into the bag 160.

Referring to FIGS. 17–20 of the drawings, a syringe comprises a syringe barrel in the form of a somewhat elongated glass vial 202, of which the bottom wall is absent apart from a slight inward projection of a strengthening bead 206 formed at the bottom of a side wall 204 of the vial and best seen in FIG. 20. In the example shown the strengthening bead 206 also has a very slight outward projection, but this is far smaller than would be necessary if the bead were formed wholly externally of the side wall 204, and may be entirely eliminated. In any event, the outward extent of the projection should be insufficient to prevent vials from standing very closely adjacent to one another without sufficient space to tip. Typically the projection will not exceed about one fifth of the total thickness of the bead. The projection of the bead on the inside should also be limited, both so that the head 210 of 1a moulded rubber piston 208 can be inserted into the vial past the projection (this is facilitated by the presence of peripheral grooves 212 in the head between sealing lands 214), and so that a sleeve 218 of a combined finger grip, piston stop and plunger guide 216 (henceforth referred to as the finger grip) can be pushed past the projection whilst remaining a snug fit within the side wall of the vial. Insertion is facilitated by the slight flare provided at the bottom e...y to the vial body by the rounding of the bead, and the insertion is readily mechanized.

The piston 208 is also provided with an integrally moulded downward extension 220 which is formed with a central cavity 223 to increase its flexibility relative to the head 210 of the piston which is substantially solid. The piston is dimensioned so that when it is in-

serted in the vial 202, the lands 214 are compressed sufficiently to form a hermetic seal against the interior of wall 204 whilst permitting the piston to be moved longitudinally of the vial. Initially, the piston is located at the bottom of the vial (see FIG. 18), with the bottom of extension 220 just within the vial so that it does not affect the ability of the vial to stand upright on its base formed by the bead 206. The location of the fairly massive solid rubber piston 208 at the base of the vial helps stabilize the empty vial 202, even when the height of the latter is somewhat greater relative to its diameter than is normally required for stability. The practical limit of the height to diameter ratio is set entirely by the requirement that the vials can be conveyed through a conventional vial filling and capping machine in a sufficient stable manner to permit reliable operation of the machine. In the example shown, the vial has an outside diameter of approximately 3 cm and a height of 12.8 cm for this diameter. A height of 14 centimeters is believed to approach the practical limit for stability, but this ratio will vary somewhat according to the relative wall thickness of the vial and the weight of the piston. Provided that the outward projection of the bead 206 is insufficient to affect stability, so that the vials can jostle without applying tipping force to each other, and assuming use of a piston generally as described, the maximum ratio attainable should be greater than 4, but will be less than 5.

The stopper 222 and cap 224 applied by the conventional vial filling and capping machinery may be of conventional construction, although the stopper 222 is preferably designed substantially to fill the neck of the vial so as to minimize dead space above the piston when the latter is pushed to the top of the vial (see FIG. 3). This ensures that as much as possible of the contents of a syringe formed from the vial can be expelled by movement of the piston.

The cap 224 is preferably modified as shown in FIG. 19 and FIG. 20. In FIG. 19, a conventional main cap cooperates with a moulded plastic adaptor assembly comprising an annular flange 226 within the cap, a cylindrical extension 228 extending through the cap and a thin diaphragm 230 closing a bottom end of the extension. An internal thread 232, similar to that provided on conventional syringe adaptors for receiving needles, such as those sold under the trade-mark LUER-LOK, is formed within the adaptor. A removable push on cap may be provided to close the open end of the adaptor during storage, being removed prior to use. In FIG. 20, the cylindrical extension 228 is formed integrally with the aluminum cap, again with an internal thread 232. I have found that the extension 228 can be accommodated by conventional vial capping machinery, at any rate with no more than minor modification, without interfering with the capping process, whilst the provision of such an extension enables the elimination of a separate adaptor cap, and the additional assembly step required to apply it.

In order to convert the vial into a syringe, either a double ended needle 234 of the blood collecting type may be applied directly to the extension 228 (see FIG. 20) or an adaptor 236 (see FIGS. 17 and 19) may be provided for any needle or alternative delivery device equipped with a standard syringe coupling so as to provide the latter with the capability of penetrating the stopper 222, as well as the diaphragm 230 if present. The adaptor 236 has a needle 238 and external thread 240 at one end, the needle providing the penetration function and the thread 240 engaging the thread 232, while its other end provides an internally threaded socket 242 and coaxial spigot 244 for forming a fluid-tight coupling to the needle or the like.

Prior to fitting the double ended needle 234, or needle and adaptor 236, a plunger 246 is applied to the extension 220 of the piston. The plunger has a shaft 248, of cruciform cross-section in the example shown, an internally threaded sleeve 250 at its one end, and an end flange 252 at its other end. The sleeve 250 has internal multistart threads 254, complementary to external multistart threads 256 on the extension 220. The lands between the threads 254 on the sleeve 250 and the threads 256 on the extension 220 both stop short respectively of the outer end of the sleeve 250 and the inner end of the extension 220 so as to form abutments 258, 260 which prevent the sleeve 250 from being screwed tightly against the underside of the head 210 of the piston. This means that any diling forces applied to the plunger are applied to the relatively flexible extension 220 and not directly to the head 210, thus minimizing the risk of breaking the hermetic seal between the head 210 and the vial.

The plunger is formed of a hinge-forming synthetic plastic such as a pharmaceutical grade polypropylene, and a generally semicircular peripheral portion 262 of the flange and is separated from the remainder of a slot 264, remaining connected only by thin, hinge-forming connections 266. This portion 262 provides a finger loop which can be pulled rearwardly, as shown by broken lines in FIG. 1, to facilitate handling of the plunger. As a supplemental or alternative feature, a notch 272 may be formed in the shaft 248 of the plunger, to provide a hook by means of which the syringe may be suspended when used in certain infusion applications.

In order to provide the various functions of preventing total withdrawal of the piston, forming a guide for the plunger and restricting its tilting movements, and providing a finger grip for the user, the combined finger grip and retainer 216 is pressed into the bottom of the vial 202 after filling and capping of the latter. It comprises the sleeve 218 and a peripheral flange forming oppositely extending finger grips 268. It is also moulded from a pharmaceutical grade of plastic such as polypropylene. The sleeve 218 is a resilient press fit in the open end of the vial 204 so that it is slightly compressed by the internal projection of the bead 206 during insertion. Insertion of the retainer 216 may be facilitated by moderate warming of at least the retainer, and the slight flare provided by the rounding of the bead 206 also facilitates insertion. Beneath the grips 268 the sleeve has shallow arcuate grooves 270 in which the bead 206 snaps as the sleeve is pressed home. Forces applied to the grips 268 tending to pull the sleeve 218 away from the vial in turn tend to deform the sleeve, in such a manner as to increase the grip of the grooves 2700 on the bead thus resisting withdrawal of the sleeve.

During manufacture, the empty vials 204 are conveyed through a conventional sterilizing station, the piston 208 is inserted in each vial 204, and the latter is filled and capped utilizing conventional vial filling and capping machinery (but preferably using a modified cap as shown in FIGS. 17 and 19 or FIG. 20). The guide and finger grip 218 is then pressed into the base of the vial, which is shipped with the plunger 246 unattached. Prior to use, the plunger 246 is screwed onto the piston, and a needle or the like is applied to the extension 228, utiliz-

ing an adaptor 236 if necessary so as to penetrate the stopper 222, at which point the syringe is ready for use.

A modified configuration of the bottom end of the vial body is shown in FIG. 21, in which an alternative approach is utilized to bringing the bead at the bottom end substantially within the diameter of the cylindrical vial body. Peripheral beads around the openings of glass bodies of this type are conventionally formed by flame softening the glass and adjusting the positioning and profile of the bead by rolling the body against suitable forming surfaces. In the FIG. 5 embodiment, a bottom portion 274 of the body 204 is flame softened and rolled so as slightly to reduce its diameter over about a length of typically 5-6 mm, and a fairly conventional outturned rounded bead 206 is formed by flaring the bottom of this reduced diameter section. The reduction in diameter is such that at least the greater part of the bead is within the general diameter of the body. In the example shown, the outside diameter of the bead is very slightly greater than the general outside diameter of the body but this need not be so. In a typical example, the inside and outside diameters of the main portion of the vial body are 27 mm and 30 mm respectively, providing a wall thickness of 1.5 mm, and the reduction in diameter at the bottom is about 1 mm. The bead can then be formed by flaring the bottom end of the vial without increasing the outside diameter of the bead significantly beyond that of the main portion of the vial and typically by no more than 0.5 mm, even though a significant flare 276 can be provided and, because of the flare, the bottom contact line 278 of the vial when free-standing on a plane surface is substantially coincident with the outside diameter of the main body 204 of the vial, thus maximizing stability. Juxtaposition of the vial bodies in the event of jostling on a line will prevent any ramping tendencies which might otherwise occur with a flared bottom configuration of this type.

Whilst the presence of the piston after its insertion in the vial body acts to introduce a substantial mass which trends to stabilize the vial, the mass of the piston relative to that of the vial body will decrease as the height of the latter increases. Nevertheless it will result in a smaller rise of the centre of gravity of the assembly as the vial becomes higher than would otherwise be the case. It is also desirable that the vial bodies be stable without the piston present so that they may be conveyed through a stabilizer prior to insertion of the pistons. The present invention is particularly valuable in this respect since the disturbing influence of a bead at the open end projecting beyond the diameter of the main portion of the body is particularly severe under such conditions.

In order to cooperate with the modified vial body profile, the finger grip/retainer 216 must also be modified. The groove 270 is replaced by a bead 280 at the upper end of the cylindrical portion 218, which bead may be moulded with a taper and if necessary with slots 282 to facilitate insertion, and/or the component 16 may be warmed to facilitate insertion. The bead must retain the component with sufficient tenacity to withstand pressures from the piston which may be developed through pressure build-up in the vial during normal storage, although it should be noted that pressure of the piston on the bead may actually help retain it by forcing it against the shoulder 284. Alternatively or additionally, claws 286 may be moulded onto the component 216 to retain it by external engagement with the bead 206.

Referring now to FIGS. 22 and 23, shell vials are a well known and widely available packaging for pharmaceutical diluents. A shell vial differs from a conventional pharmaceutical or serum vial in that it has no neck. Instead the top of the vial is of the same diameter as the remainder of the cylindrical side wall of the vial, and is closed by a piston quite similar to that utilized by the present applicant to close the bottom of his bottomless vial.

FIG. 22A shows an exploded view of the components of a separately assembled and sterilized unit 300 for use in conjunction with a filled and capped vial 302 similar to that shown at the right of FIG. 12. The unit 300 comprises a shell vial having a cylindrical body 304 closed at one end, and a piston 306 closing its other end to enclose a quantity of pharmaceutical diluent. A moulded plastic tubular adaptor component 308 having a tubular connector 310 at one end similar to the connector element 700 of FIG. 12, and an internal thread 312 within its other end is engaged with an external thread on a extension 314 of the piston 306. The unit further includes a tubular plunger 316 similar to the plunger 10 of FIG. 12, a cap 318 similar to the cap 2 of FIG. 12, a needle 320, and a protective cap 322 which closes the open end of the cap to maintain sterility and provide protection of the needle during storage. This cap is removed immediately before use (see FIG. 22C). The needle 320 is of the double ended type, and is located beneath the cap 318 by a flange 324. A connector 326 on the cap similar to the connector 27 of FIG. 12 engages the connector 310 on the adaptor component 308 in the same way as the connector 27 engages the connector 70 in FIG. 12, so that one end of the needle 320 passes through the adaptor towards the piston extension 314, as seen in FIG. 22B.

After the cap 22 has been removed (FIG. 22C), and also a flip-off protective cover 328 on the cap of the vial 302 (FIG. 22D), the unit 300 is pressed on the vial 302 (FIG. 22E) so that the cap 318 is pressed over the cap 330 of the vial 302 so that the lower end of the needle 320 pierces the closure of the vial 302. At the same time, the flange 324 is pressed upwardly within the cap 318 and causes the upper end of the needle 320 to penetrate a septum within the piston 306.

The shell vial 304 is then pressed downwardly (FIG. 22F) expelling its contents through the needle 320 into the vial 302. If necessary, the piston 332 within the vial 302 is positioned higher in the vial than normal so that it can be displaced downwardly to make room for the contents of vial 304 (see FIG. 22G).

At this point, the assembly 300, with the exception of the cap 318 and the needle 320, is pulled away from the vial 302 by gripping the plunger 316 leaving the cap and needle in place on the vial (FIG. 22G). The plunger 316 is then screwed onto the piston 332 of the vial 302 (FIG. 22H) to form a syringe 334 (FIG. 22I).

In the embodiment just described, the shell vial is dimensioned so as to fit within the tubular plunger. An alternative embodiment is shown in FIGS. 23A-G in which the shell vial 304 is dimensioned so that the tubular plunger 316 has an external diameter less than its internal diameter. The same reference numerals are used to denote components of this embodiment similar to those of FIG. 22A-I, and only the differences will be described. In this instance, the plunger 316 fulfils the functions of the adaptor 308, the screw threads on the pistons 306 and 332 being similar except that the thread 314 on piston 306 may be longer. The plunger 316 is a

press fit on the connector 326 on the cap 318, which in this case is formed with a skirt 336 which fits over the top portion of the vial 302 and also provides a finger grip 338. The entire unit 300 (see FIG. 23C) is assembled into a tubular sleeve 340 (FIG. 23B) which together with the cap 322 maintains sterility of the unit during storage, and also facilitates preparation of the syringe. The vial 304 is a press fit within the upper end of the sleeve 340. After removal of the cap 322, the unit 300 is applied to the vial (FIG. 23D) as in the previous embodiment, and the sleeve 340 is pulled downwardly (FIG. 23E). As before, this forces the cap 318 onto the cap 330 of the vial, causing the needle 320 to pierce both the closure of the vial 302 and the piston 306 of the shell vial 304, and further downward movement of the sleeve 340 forces the contents of the shell vial into the vial 302. At this point the sleeve 340 is rotated to unscrew the piston 306 of the shell vial 304 from the plunger 316 (FIG. 23F) which is then transformed to the piston 332 to complete the syringe.

It should be understood that the sleeve 340 could be omitted, although it is a convenience for packaging and manipulating the syringe, in which case the vial 304 would be manipulated directly rather than through the sleeve 340.

Variations in the above embodiments are possible. For some applications of the syringe, it may be desired to replace the needle 320 by some other instrumentality when the syringe is used, in which case a single ended needle may be located in the assembly 300 so that it will be forced upwardly as the cap 318 is forced onto the vial 302 (the cap in this case will have an internal cannula to piece the closure of the vial), but will be retained within the shell vial when the latter is removed during preparation of the syringe. If a double ended needle 30 is used, in combination with a cannula, venting of the vial 302 to permit escape of air displaced by the contents of the shell vial 304 becomes possible, in a manner similar to that shown in FIG. 16.

A sleeve similar to the sleeve 340 may also have utility in packaging and manipulating subassemblies for other embodiments of the invention incorporating push-on external caps for the vial similar to the cap 318.

I claim:

1. In a method of packaging a pharmaceutical in a pharmaceutical vial formed of rigid transparent material with a cylindrical body and a comparatively wide open neck at the top of the body, which method comprises conveying uncapped vials, empty of pharmaceutical, in a free-standing upright position through vial filling and capping machinery which fills the pharmaceutical into the body through the open neck, applies an elastomeric closure to the open neck, and applies a cap overlaying the closure to secure the closure to the neck to produce filled and capped vials, the improvement in which, in order to permit subsequent administration via injection direct from the vial, a cylindrical side wall of each uncapped empty vial is formed so as to define a bottom opening at the base of the vial with a bead adjacent to the bottom opening, the outer wall of the vial being free of any external projection of the bead relative thereto sufficient to cause substantial instability of the vial when conveyed upright and free-standing adjacent to other similar vials during filling and capping, and a cylindrical substantially solid piston of resilient material is slidably lodged prior to filling of the vial wholely within the cylindrical side wall above said bottom opening so as to form a hermetic seal with the side wall, so that an internal and axial extension from the piston, of lesser diameter than the piston and adapted for subsequent coupling to a syringe plunger, is oriented so as to extend downwardly within the vial towards the bottom opening.

2. A method according to claim 1, including the further step, following filling and capping, of snap fitting a piston stabilizer ring to the bead so that flanges on the piston stabilizer ring extend into the body between the cylindrical side wall and the piston extension to prevent escape of the piston from the body.

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United States Patent [19]

Sams

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[54] **MEASURED DOSE DISPENSING DEVICE**

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[57] **ABSTRACT**

The present invention relates to a device for dispensing a fluid from a container by means of the axial movement of a piston within the container under the influence of a plunger moved by the device, which device is adapted to receive the container on its forward end and to move the plunger axially forward towards or within the container so as to dispense a selected amount of fluid from the container upon each actuation of the device, characterized in that the device comprises:

i. a disengageable drive mechanism adapted to be reciprocated axially of the device and adapted to positively engage the plunger whereby the plunger can be moved axially forward by the drive mechanism and to be disengaged from the plunger to permit relative axial movement between the drive mechanism and the plunger;

ii. a disengagement means for selectively engaging or disengaging the drive means from the plunger;

iii. an actuating means, which may be integral with or separate from the disengagement means, for actuating the disengagement means, which actuation means requires a positive operation from a user of the device to engage and/or disengage the drive mechanism from the plunger; and

iv. means for selecting the extent of travel of the drive mechanism so as to control the extent of axial movement of the plunger upon actuation of the device.

The invention also provides a device of the invention in association with a container of the fluid to be dispensed.

19 Claims, 4 Drawing Sheets